

Biomedical Instrumentation

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Biomedical Instrumentation

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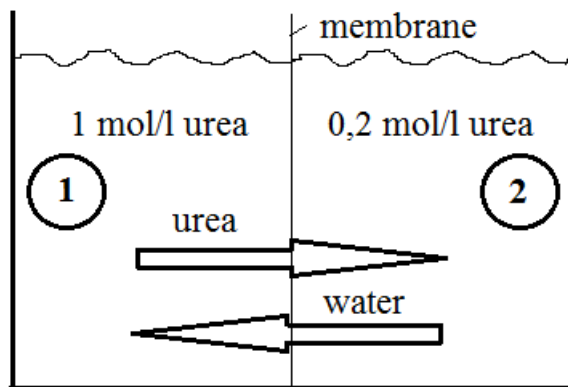
Chapter 1. Biopotentials: origin and electrodes

The basic building block of human body is the *cell*. Membrane isolates but also connects the internal part of the cell to the external environment. Biopotentials result from the process across the cell membrane of certain – excitable – cells. Below we analyse processes across (semi)permeable membranes.

1. Diffusion of uncharged molecules

Consider a container with two chambers of equal volume. The chambers are separated by a cellophane membrane, see Fig.1.1. Chambers contain uncharged molecules (e.g. urea), in chamber 1 the concentration is 1 mol/l, in chamber 2 0.2 mol/l [1.2].

Figure 1.1. Transport between two chambers separated by a membrane



Cellophane membrane is permeable for both urea and water molecules. Urea molecules will move through the holes in the cellophane membrane from chamber 1 to chamber 2, i.e. from greater concentration to lower one. This process is called diffusion. Urea molecules are moving around in the solution. When they reach the cellophane membrane they can get through it to the other chamber. From the chamber where the urea concentration is greater more molecules will get to the chamber with lower concentration. (However, some molecules will move from the chamber with lower urea concentration to the chamber with higher concentration!) The diffusion process ends when the urea concentration in the two chambers will be equal, in the above mentioned case 0.6 mol/l. Fick's first law of diffusion describes the process (eq. 1.1) :

$$J_d = -D \frac{dC}{dx} \quad (1.1)$$

where J_d is the diffusion flux [the unit is (mol/cm²)/s], D is the diffusion constant [the unit is cm²/s] and dC/dx is the concentration gradient [the unit is (mol/cm³)/cm]. The diffusion constant D is:

$$D = \frac{RT}{f} \quad (1.2)$$

where R is the gas constant [8.31 (J/°K)/mol], T is the absolute temperature and f is the frictional coefficient [the unit is (J/mol) (s/cm²)], characterising how easily gets a molecule through the membrane Substituting (1.2) into (1.1):

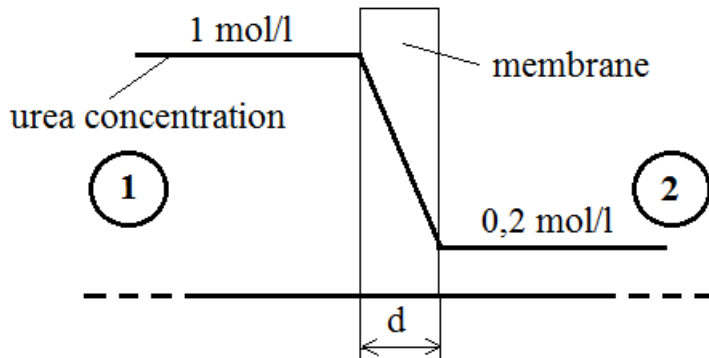
$$J_d = -\frac{RT}{f} \frac{dC}{dx} \quad (1.3)$$

Let the thickness of the membrane be d . Considering a constant concentration gradient within the membrane (see Figure 1.2) instead of dC/dx we can write $([C_1] - [C_2])/d$, where $[C_1]$ and $[C_2]$ are urea concentrations in the two sides of the membrane. The diffusion flux can be written as

$$J_d = -P_u([C_1] - [C_2]) \quad (1.4)$$

where P_u (equal to D/d , the unit is cm/s) is the permeability of the membrane to urea. The permeability of a membrane to various molecules can be rather different.

Figure 1.2. Concentration gradient in the membrane



2. Osmotic pressure

Biological membranes usually have high permeability to water. Analysing the process described in section 1.1 we have to realise that a concentration gradient does exist for water molecules. The reason is that the number of water molecules is initially different in the two chambers. As a result water molecules will also move from one chamber (where urea concentration is higher and thus 'water concentration' is lower) to the other. The movement of water molecules resulting from the different water concentration is called osmosis. If the volume of the two chambers separated with a membrane is constant then the pressure in the chambers will cause different pressure in the chambers. The pressure difference gives rise to movement of water molecules opposite to osmotic. The two effects will result in a dynamic equilibrium state. The corresponding pressure is called osmotic pressure. The osmotic pressure that results from the osmotic movement of one type of molecules can be calculated using the van't Hof equation:

$$\pi = RT([C_1] - [C_2]) \quad (1.5)$$

where R is gas constant [the unit is $0,082 \text{ (l)(atm)/(mol)(}^\circ\text{K)}$], T is absolute temperature, C_1 and C_2 [in unit mol/l] are the concentrations of the given molecule on the two side of the membrane, thus pressure π is in atmosphere. It must be taken into account that activity and concentration of the solution are equal only for dilute solutions. In general, activity (a) should be used instead of concentration (c), see eq. 1.6.

$$a = \phi c \quad (1.6)$$

ϕ is the activity coefficient, it can be between 0 and 1.

Let's calculate the osmotic pressure across the membrane of a red blood cell (corpuscles) when it is in distilled water. The cytoplasm is supposed to contain salt with 0.165 mol/l concentration. At room temperature the pressure across the membrane is:

$$\pi = RT([C_1] - [C_2]) = 0.082 \cdot 298 \cdot (0.165 - 0) = 4 \text{ atm} \quad (1.7)$$

The membrane will not be able to withstand such a high pressure. The cell volume will increase trying to decrease pressure but will rupture finally.

3. Movement of ions

The two chambers separated with a membrane now contain also ions, i.e. charged particles. Suppose the concentration of KCl is 1 mol/l in chamber 1 and 0.3 mol/l in chamber 2 and the membrane only permeable to K^+ ions. K^+ ions will move from chamber 1 to chamber 2. This means chamber 2 will be more positive than

chamber 1, there will be an electronic potential across the membrane. The potential increases as diffusion continues. Dynamic equilibrium state will be reached when the electric potential results in ionic movement equal to but opposite to that resulting from concentration difference. Not many ions have to move across the membrane to reach the equilibrium state. The ionic movement resulting from the potential difference is:

$$J_e = -\frac{dV}{dx}(zCF)\frac{1}{f} \quad (1.8)$$

where zF is the charge on a mole of ions, C is ion concentration, F is Faraday's constant (96500 C/mol), f is frictional coefficient (see section 1.1) and dV/dx is the electric field. In equilibrium state the diffusion flux J_d equals the electrical flux J_e :

$$-\frac{RT}{f} \frac{dC}{dx} = \frac{dV}{dx}(zCF)\frac{1}{f} \quad (1.9)$$

rearranging:

$$dV = -\frac{RT}{zF} \frac{dC}{C} \quad (1.10)$$

Integrating both sides:

$$V_1 - V_2 = -\frac{RT}{zF} \ln \frac{C_1}{C_2} \quad (1.11)$$

1.11 is called Nernst equation. Substituting R , z and F , on room temperature ($T = 298$ °K) we get:

$$V_1 - V_2 = (-58\text{mV}) \lg \frac{C_1}{C_2} \quad (1.12)$$

Instead of f the ion mobility μ can be used:

$$\mu = \frac{DF}{RT} \quad (1.13)$$

where μ is the mobility of the univalent ion [in unit (cm/s)(V/cm)], R is gas constant, T is absolute temperature and F is Faraday's constant. The mobility of an ion characterizes its speed in a given material due to electrical field. Ion mobility is inversely proportional to frictional coefficient:

$$\mu = \frac{F}{f} \quad (1.14)$$

In general the membrane is permeable to several ions. Suppose the HCl concentration is 0.06 mol/l in chamber 1, and 0.02 mol/l in chamber 2. The chambers are separated by a filter permeable for both H^+ and Cl^- ions. Both hydrogen and chloride ions will move from chamber 1 to chamber 2 until the concentration in both chambers will be 0.04 mol/l and there will be no potential difference across the membrane.

In the beginning of the diffusion process there will be potential difference across the membrane. The mobility of hydrogen ions is much higher than the mobility of chloride ions. As a result, hydrogen ions will get further in the membrane than chloride ions (both ions start from the surface of the membrane). This builds up an electrical field which speeds up chloride ions and slows down hydrogen ions. The so called diffusion potential:

$$V_1 - V_2 = \frac{\mu_a - \mu_c}{\mu_a + \mu_c} 58 \lg \frac{C_1}{C_2} \quad (1.15)$$

where μ_a and μ_c are the mobility of anions and cations, C_1 and C_2 are the initial concentrations in the two chambers. Although the diffusion potential changes as diffusion progresses; the change will be slow if the diffusion flux is negligible compared to the volume of the chambers. Biological membranes are permeable for most of anions and cations but their permeability is different to different ions. Taking all these into account we

get the Goldman equation [1.6] (1.16). The most important three ions in case of cells are sodium, potassium and chloride.

$$V_1 - V_2 = -58 \lg \frac{P_{Na}[Na]_1 + P_K[K]_1 + P_{Cl}[Cl]_2}{P_{Na}[Na]_2 + P_K[K]_2 + P_{Cl}[Cl]_1} \quad (1.16)$$

where P_X is the permeability to X ion, $[X]_1$ and $[X]_2$ are the concentration of X ion in chamber 1 and 2. The squid axon is often used in laboratory examinations because of its size. The inner side of the squid axon is accessible thus potential across the membrane can be measured. We can neglect Cl^- as Na^+ and K^+ ions have much higher influence on the potential difference. The axon is filled with a solution: Na^+ concentration is 50 mM, K^+ concentration is 400 mM. For the solution outside the axon: Na^+ concentration is 440 mM, K^+ concentration is 20 mM. These values are close to real concentrations when the cell is at rest. If there were only Na^+ ions on both sides of the membrane, according to eq. 1.16 these concentration values would result in a +55 mV membrane potential. The potential would be -76 mV if there were only K^+ ions. The measured potential is -70 mV. Substituting the Na^+ and K^+ concentrations (supposing Cl^- concentration is zero) and the measured -70 mV into eq. 1.16 we can calculate the ratio of permeabilities, and get $P_K/P_{Na} \sim 90$. The big difference in permeabilities explains why the measured potential is so close to the potential we would measure if only K^+ ions were present.

The thickness of the membrane is a few times ten Å. As a result, the electrical field is strong. Assuming 70 mV resting potential and 70 Å thick membrane; the electrical field is 100 kV/cm! The electrical breakdown of air is 20 – 40 kV/cm (depends on the pressure). The breakdown voltage for dry paper is about 30 kV/cm, for Bakelite is about 150 kV/cm.

We can estimate the capacity of cell membrane by considering it a planar capacitor. The capacitance per unit area is (see eq. 1.17):

$$\frac{C}{A} = \epsilon_0 \epsilon_r \frac{1}{d} \quad (1.17)$$

where C/A is the capacitance per unit area, ϵ_0 is the permittivity of vacuum, ϵ_r is the relative permittivity of the membrane and d is membrane thickness.

4. Action potential

As a result of electrical, chemical or mechanical excitation, the resting state of the cell changes. When excitation exceeds the threshold level then across the membrane we can measure a so called action potential. Its shape does not depend on the excitation [1.4]. In physiological practice it is called „all-or-nothing“. During the action potential within relatively short time (a few ms) the permeability of the membrane to Na^+ and K^+ ions changes orders of magnitude, see Figure 1.3. As a result, inside the cell the Na^+ concentration temporarily increases. Within a few milliseconds the permeability of the membrane to Na^+ and K^+ returns to the values characterising the resting state. The sodium-potassium pump then brings the Na^+ ions back outside the cell. In one cycle the Na-K pump transfers 3 Na^+ ions out of the cell and takes 2 K^+ ions into the cell. By decreasing the number of positive ions inside the cell, the pump contributes to set the resting potential of the cell negative. The transport is against the concentration gradient, ATP provides the necessary energy. During the action potential the cell neglects further excitations. This is called *refractory period*. A simple electrical model of the membrane is given in Figure 1.4.

Figure 1.3. Action potential (solid line), and the change in permeability of the cell membrane to Na and K (dashed lines)

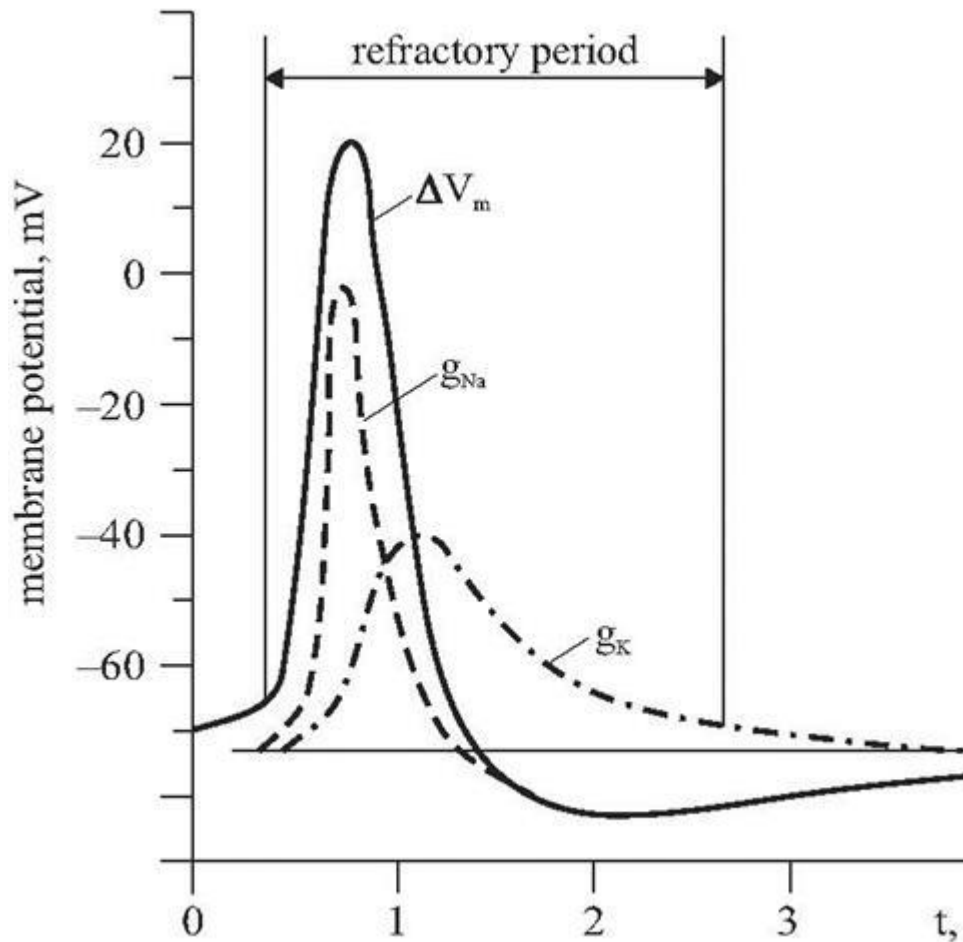
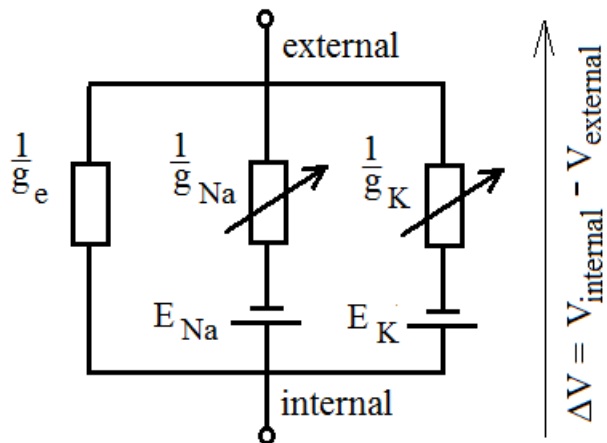


Figure 1.4. Simple electrical model of the cell membrane



5. Electrodes to measure biopotentials

Half-cell potential

In living organisms ions migrate. In the devices that process biopotentials current means moving of electrons. The primary task of a biopotential electrode is to convert ionic current into electron current. This is illustrated by the animation at http://project.mit.bme.hu/kobak2012/ionic_to_electronic.pps

When metal is immersed into electrolyte then a so called half-cell potential will develop across the interface [1.5]. Table 1.1 gives half-cell potentials for a few metals. The reference is a so called reference electrode [1.7], e.g. $\text{Pt}(\text{H}_2)\text{H}^+$.

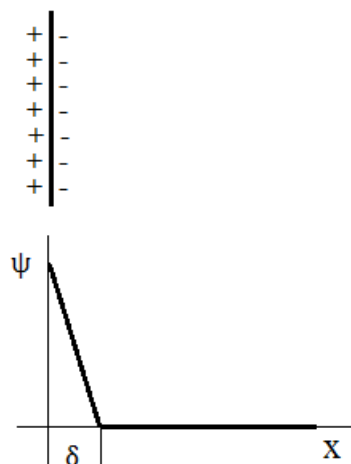
Table 1.1. Half-cell potential values for a few metals

metal and reaction	half-cell potential on 25 °C (V)	temperature coefficient (mV/°C)
$\text{Al} = \text{Al}^{3+} + 3\text{e}^-$	-1.662	+1.339
$\text{Zn} = \text{Zn}^{2+} + 2\text{e}^-$	-0.7628	+0.962
$\text{Pt}(\text{H}_2)\text{H}^+$	0	-
$\text{Ag} + \text{Cl}^- = \text{AgCl} + \text{e}^-$	+0.2225	+0.213
$\text{Au} = \text{Au}^+ + \text{e}^-$	+1.691	-

When metal is immersed into electrolyte, it changes the distribution of charged particles around the interface [1.8]. There are different models to describe the phenomenon. The Helmholtz-model (Figure 1.5) is the simplest one. It is adequate for most cases related to biopotential measurement.

The half-cell potential cannot be measured directly. If we immersed a metal conductor into the solution to measure the half-cell potential across the interface there would be another half-cell potential and we would measure the difference of the two. When two identical metal electrodes are immersed into the solution, the potential between the two electrodes should be zero. The potential different from zero is noise. The noise of an electrode is greatly increased by contamination caused by another metal. The effective value of noise is around 0.01 mV for pure copper or silver electrodes, while for a silver electrode contaminated by copper the value can be 0.2 mV.

Figure 1.5. The Helmholtz model depicts the distribution of charged particles around the electrode-electrolyte interface



D'Arsonval introduced the silver electrode coated with chloride in 1880. This electrode – misleadingly called non-polarisable – also develops half-cell potential, but its value is stable. As a result, the potential difference between two identical electrodes immersed into the same electrolyte is negligible.

6. Electrode models

At the electrode-electrolyte interface anions and cations (i.e. charged particles) are separated. This is the property of a capacitance. The distance between the 'plates' of the capacitance are very close to each other, thus the capacitance per unit area is relatively high. The build-up is similar to the electrolytic capacitor. Figure 1.6 refers to the usual case when biopotential is measured using an electrode pair. The figure shows an electrical model and the impedance that can be measured between the electrodes. The impedance is frequency dependent. Warburg suggested DC voltage sources (E_a and E_b), and resistors in series with capacitors (R_a , C_a and R_b , C_b). The DC leakage current across the electrode-electrolyte interface is modelled by R_{fa} and R_{fb} . The resistance and

capacitance per unit area depends on frequency as well as on current density [1.1]. Figures 1.7 and 1.8 illustrate this dependence for stainless steel electrodes. As the frequency increases, both resistance and capacitance per unit area decrease. At greater current densities the resistance per unit area decreases while capacitance per unit area increases.

Figure 1.6. Model for the electrode-electrolyte interface

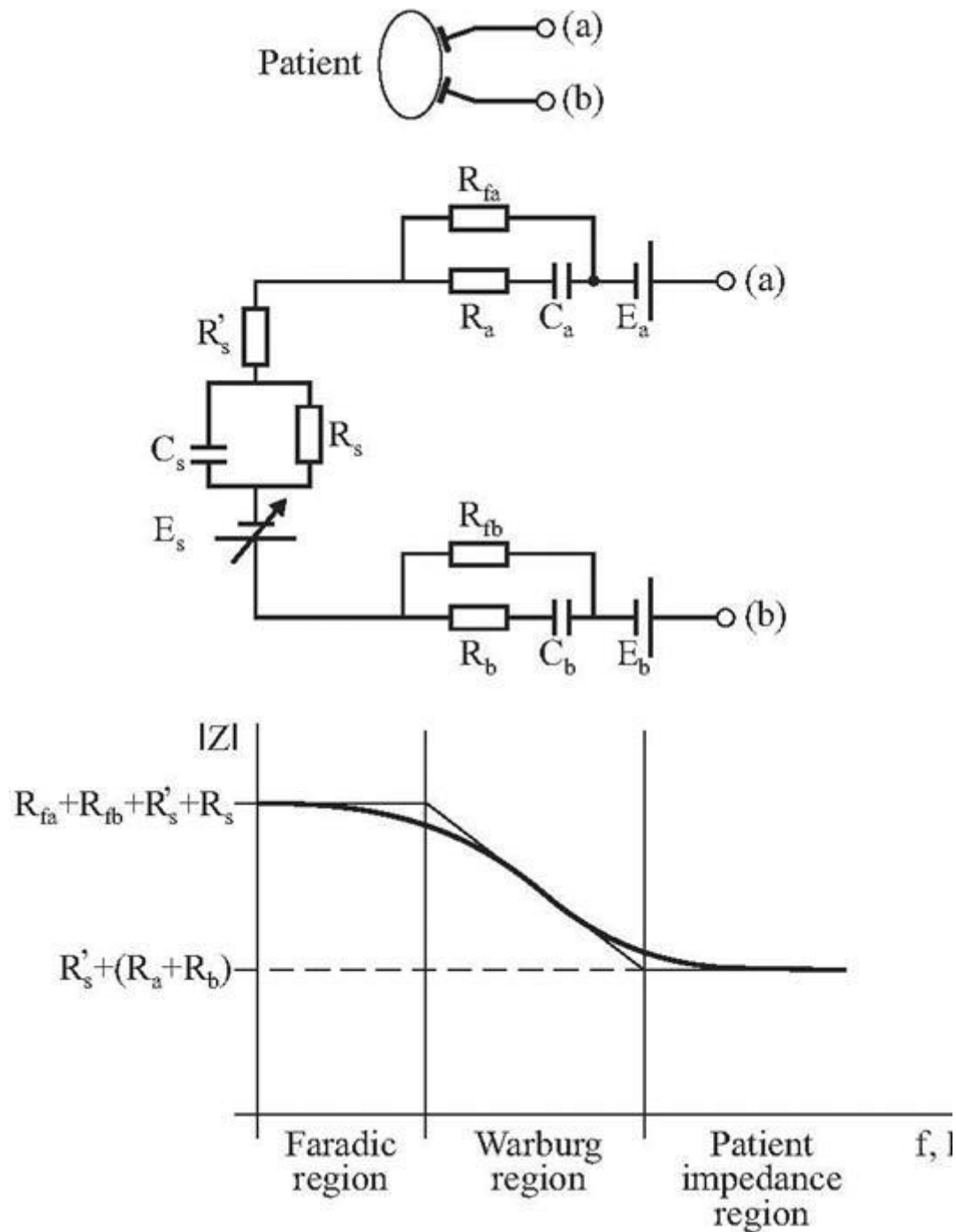


Figure 1.7. Impedance vs. frequency for stainless steel electrode

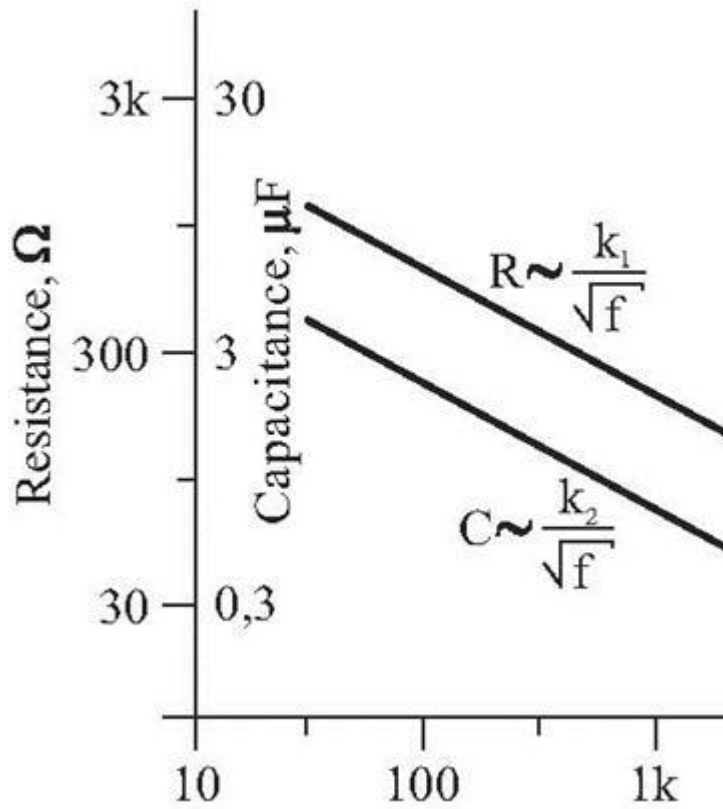
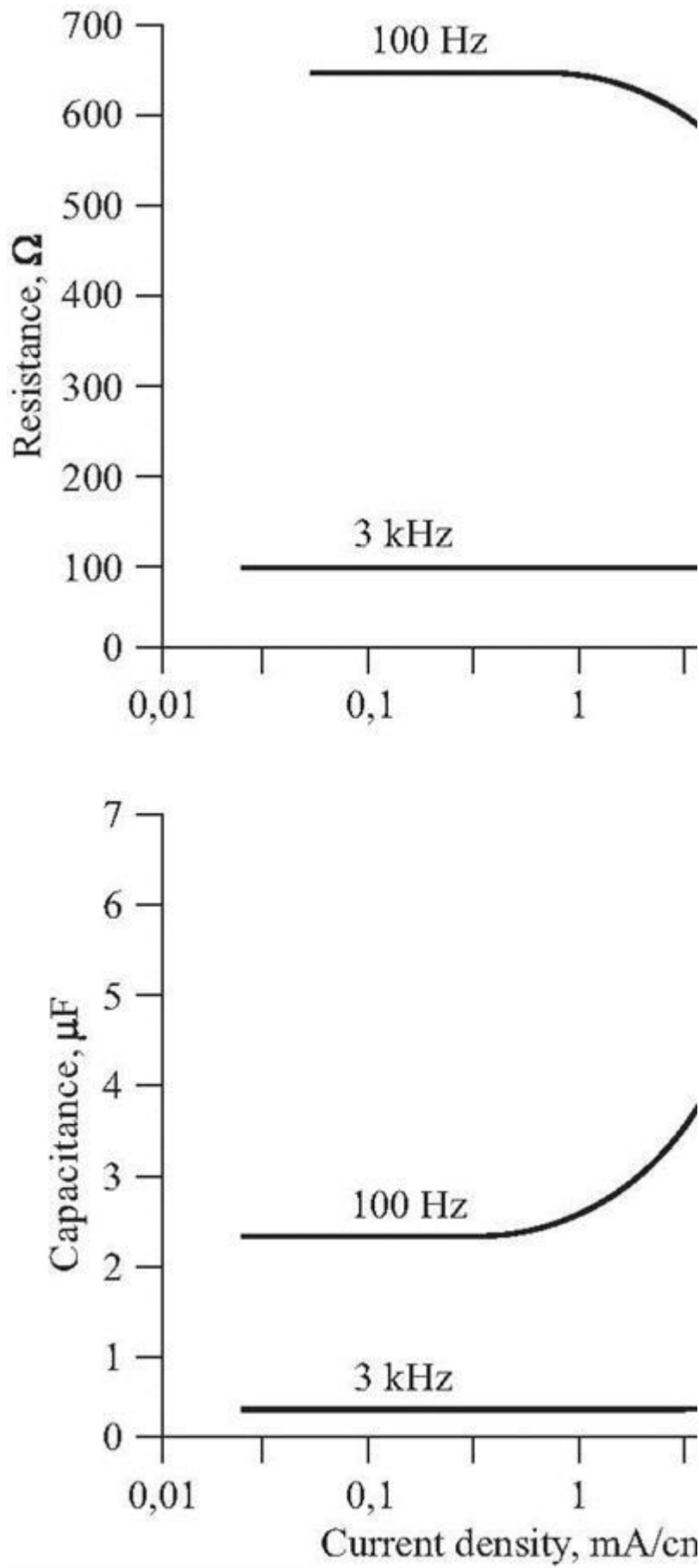
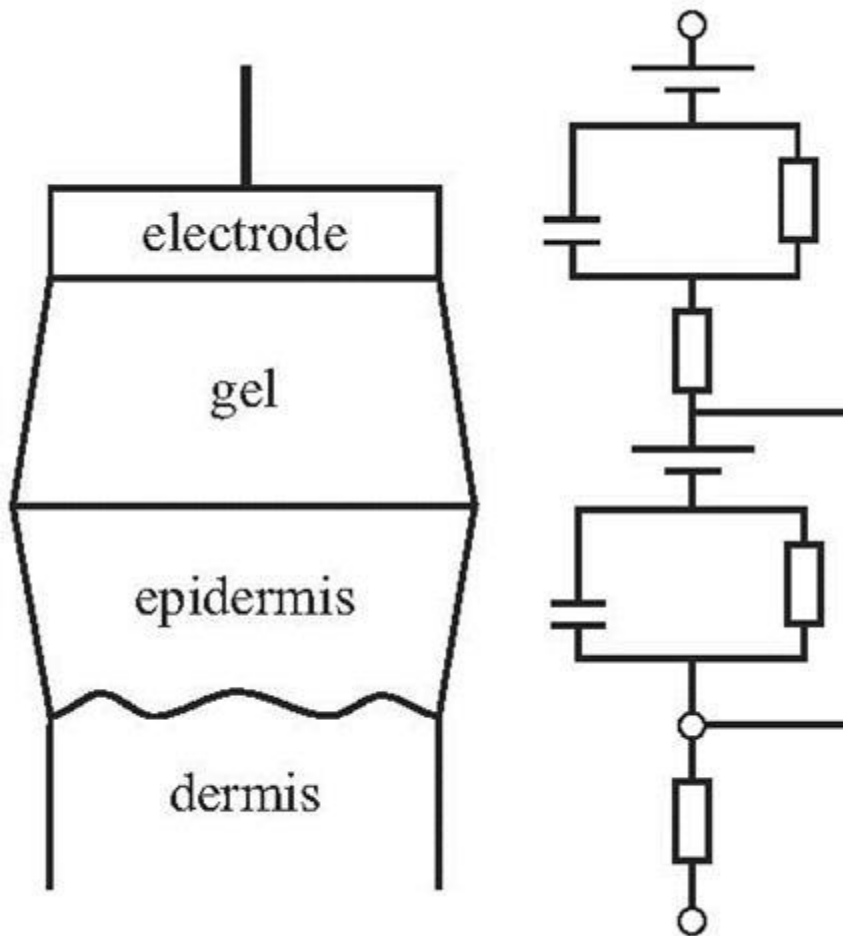


Figure 1.8. Impedance vs. current density for stainless steel electrode



Skin is made up of several layers. Figure 1.9 gives a possible model for the electrode-skin interface.

Figure 1.9. Model for the electrode-skin interface



7. Electrode polarization

When we use two electrodes to measure biopotentials, the current flowing through them causes polarization overvoltage (eq. 1.18):

$$V_p = V(i) - V(0) \quad (1.18)$$

where V_p is the polarization overvoltage, $V(i)$ is the difference of half-cell potentials when current i is flowing, $V(0)$ is the difference of half-cell potentials when no current is flowing. There are two basic types of frequently used electrodes.

$V_p = 0$. These are called non-polarisable or reversible electrodes, such behaviour is shown by silver-silver chloride and calomel electrodes. The energy level needed to deposition or dissolution is low; the current density can be high across the interface.

$V_p = V_{\text{applied}}$. These are called polarisable or irreversible electrodes, platinum electrodes show very similar behaviour. Applying voltage to the electrode pair immersed into electrolyte no current flows, the applied voltage will drop across the electrode-electrolyte interface altering energy levels needed to deposition and dissolution. If we apply AC voltage, current flows between the electrodes showing their capacitive character.

For biopotential electrodes the polarization overvoltage has three components: $V_p = V_r + V_c + V_a$. Indices refer to resistive (r), concentration (c) and caused by the change of activation energy levels (a).

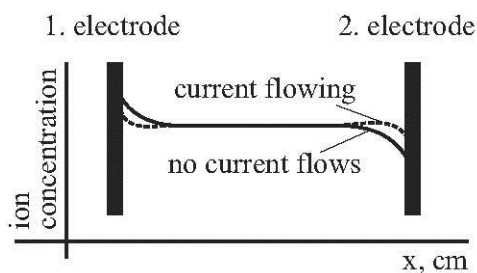
Resistive overvoltage

All electrode-electrolyte interfaces have certain impedance. The impedance is not purely ohmic and depends on the direction and density of the current. Its value can be decreased by increasing the surface of the interface. The so called sintering process is based on atomic diffusion. The silver-silver chloride electrode has high interface area. This is reached by sintering: silver is granulated, mixed with silver powder and chloride, heated and pressed on silver wire. Similar method is used for platinum electrodes. Platinum grating is pressed on thin platinum plate. Simple method is to increase the electrode surface to decrease its impedance. However, in biomedical practice the increase of electrode surface is limited.

Concentration overvoltage

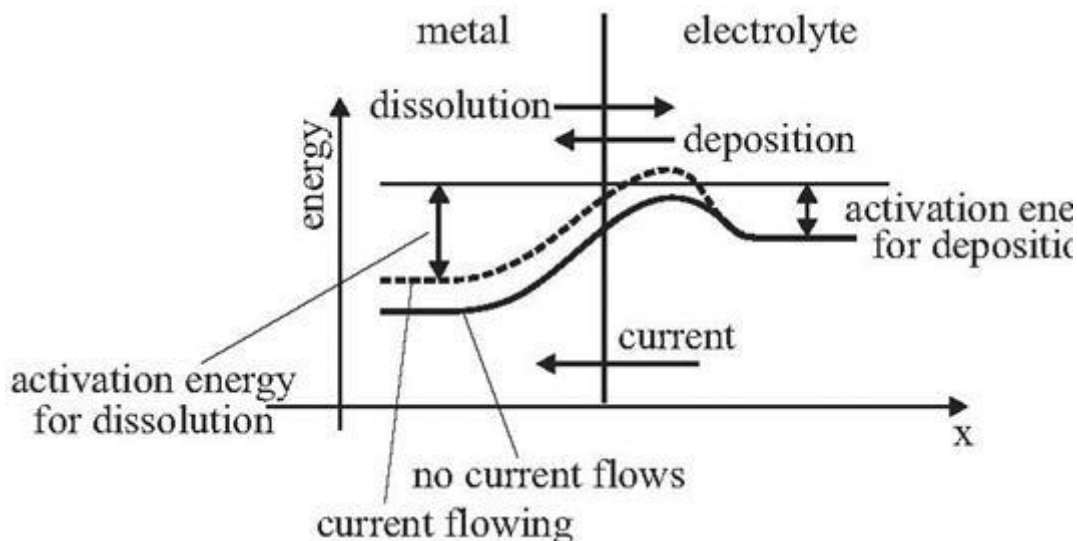
Immersed metal electrode alters the ion concentration distribution in electrolyte. Current flowing through the electrodes also changes the distribution of ions (see Figure 1.10). This will modify the voltage between electrodes.

Figure 1.10. Polarization overvoltage caused by concentration difference

*Overvoltage caused by the change in activation energy levels*

Activation energy levels (barriers) needed for deposition and dissolution determine the current that can flow across the electrode-electrolyte interface. The energy levels are modified by the applied external voltage (see Figure 1.11). Change in activation energy levels is the major source of polarization overvoltage.

Figure 1.11. The change of activation energy levels is the major cause of polarization overvoltage



8. Electrode types (macroelectrodes)

Disposable electrodes (see Figure 1.12) are cheap (unit price is around 0.05 €), their application is economical. Electrodes do not have to be sterilized, aging does not exist.

Figure 1.12. Disposable electrodes with adhesive ring

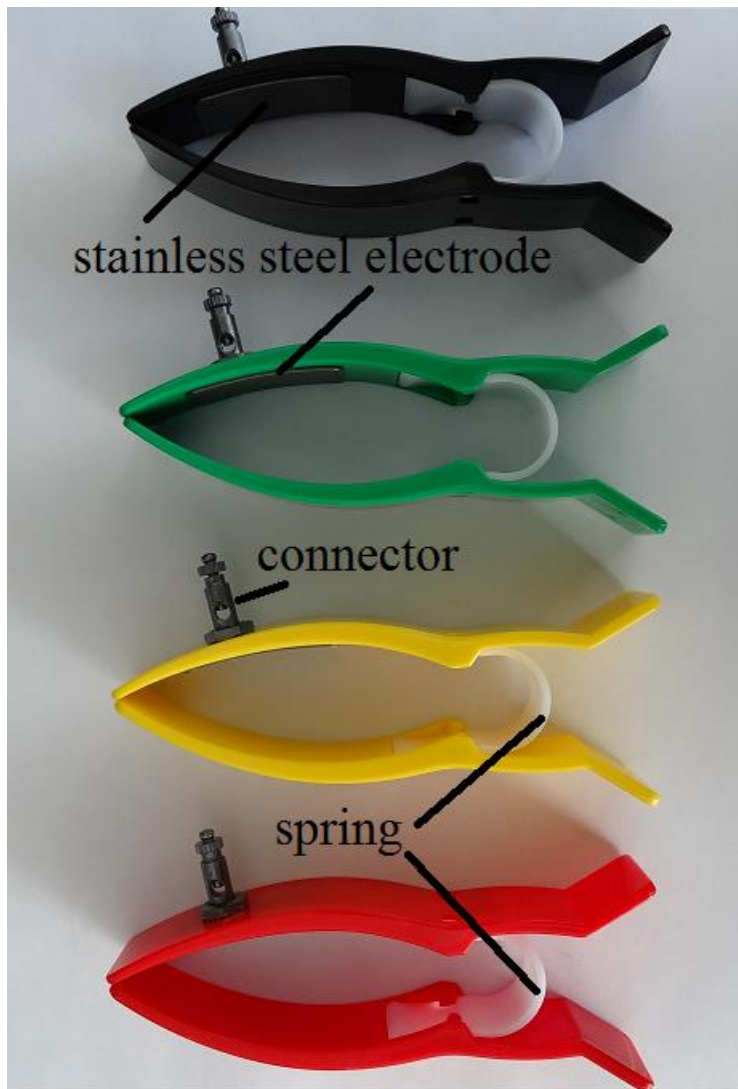


Figure 1.13. ECG chest electrodes



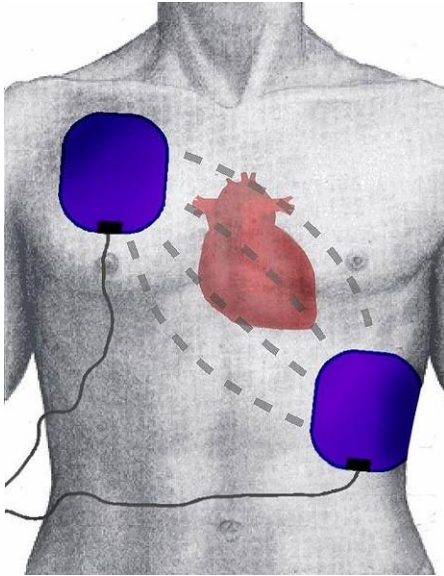
Chest electrodes for ECG recordings have a sucking balloon (see Figure 1.13). Limb ECG electrodes are colour coded: red (right arm), yellow (left arm), black (right leg) and green (left leg). Limb electrodes are available for children.

Figure 1.14. ECG limb electrodes



Defibrillation requires high current density thus the applied electrodes have large area. The size and placement of electrodes are demonstrated in Figure 1.15.

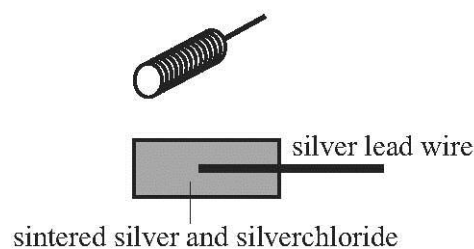
Figure 1.15. Electrode placement for defibrillation
(http://commons.wikimedia.org/wiki/File:Defibrillation_Electrode_Position.jpg, author: PhilippN)



Silver-silver chloride electrode

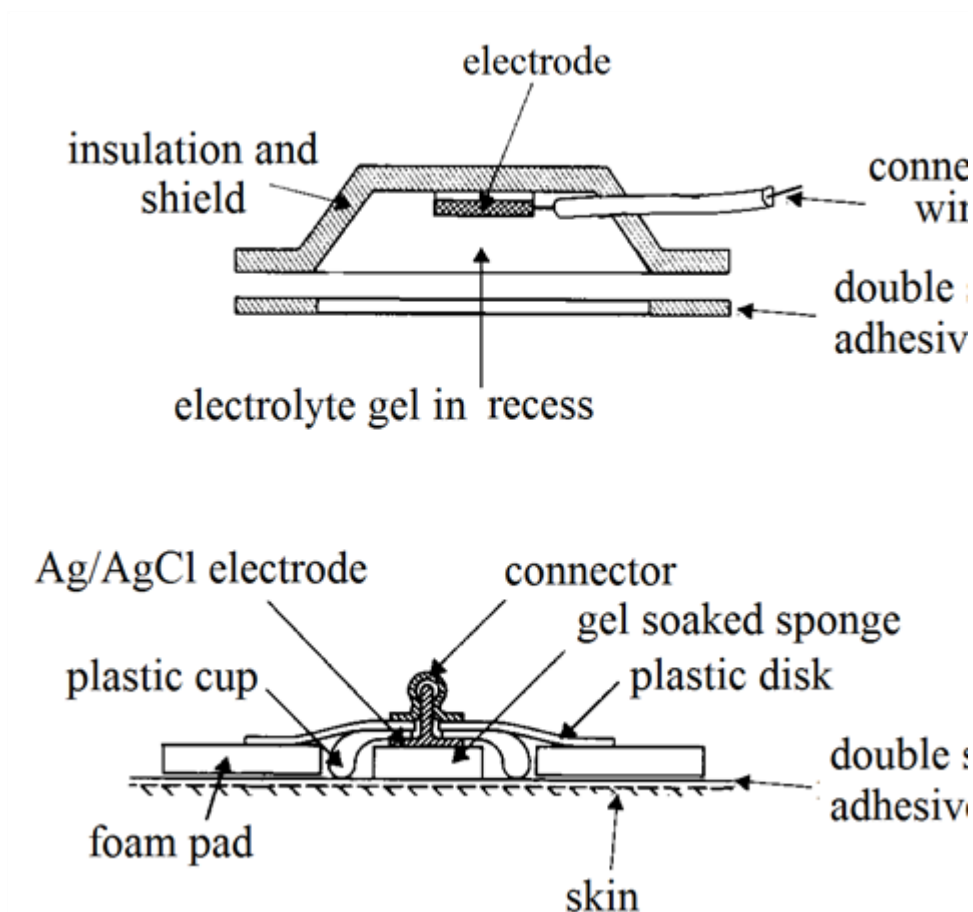
Silver-silver chloride is the most widespread electrode. The interface and transfer between ionic/electronic current is inside the electrode (see Figure 1.16), thus the half-cell potential is stable and the noise is small. This type is close to the ideal non-polarisable electrode, it can be used to measure DC current, too. Further advantage is its simple producibility. The electrode impedance has minimum value at a certain chloride thickness. When DC current flows through an electrode pair (see Figure 1.6) chloride will deposit on the positive electrode and dissolve from the negative one. As a result the electrical characteristics of the electrodes will change. As the chloride coating becomes thinner the electrode starts to become polarisable. Small noise requires nearly pure silver (99.99 - 99.999 %).

Figure 1.16. Construction of the silver-silver chloride electrode



Silver-silver chloride electrode is light-sensitive. Recessed electrodes (see Figure 1.17) shade the light-sensitive part. They use electrolytic fluid or gel to connect the electrode to the skin, thus reducing motion artefact.

Figure 1.17. Disposable (below) and reusable (above) silver-silver chloride electrode structures



Platinum electrode

The energy levels needed for deposition and dissolution are extremely high, thus platinum electrodes are nearly ideal polarisable.

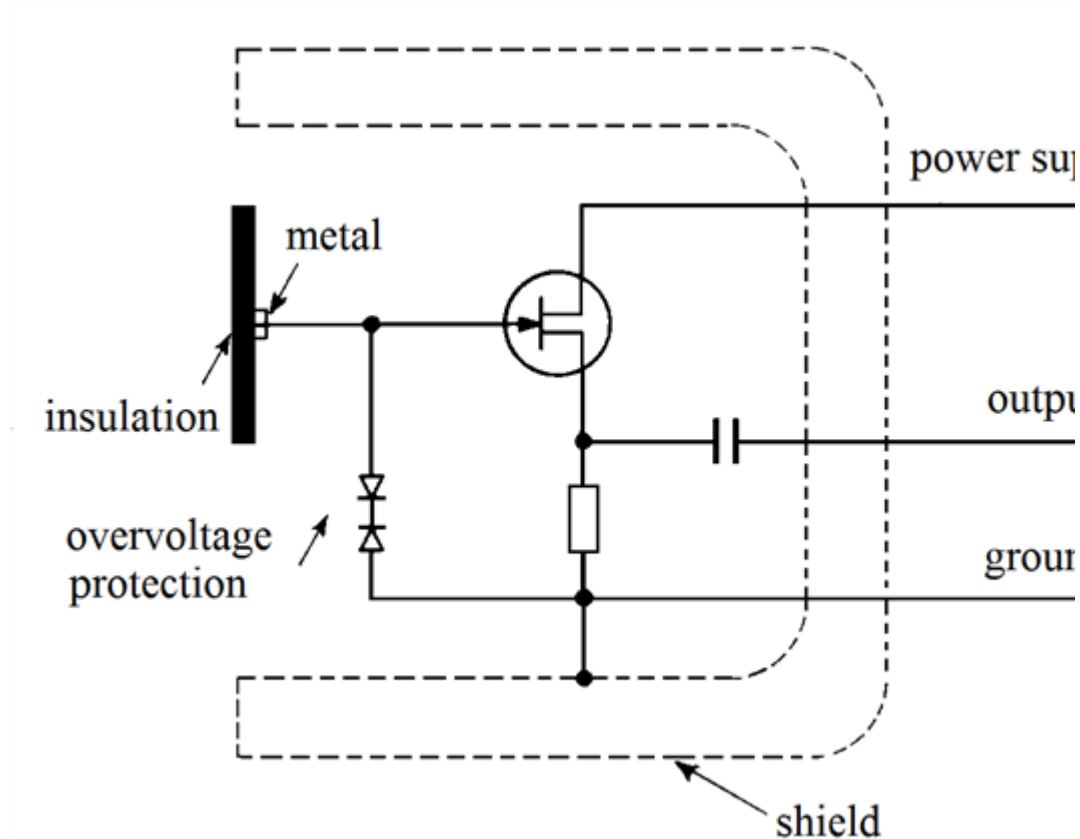
Stainless steel electrodes

It is simple and cheap, easily sterilisable and reusable. Widely used ECG limb electrodes (Figure 1.14) and chest electrodes (Figure 1.13) are made of stainless steel.

Active electrode

They connect to the body surface through capacitive coupling. A possible construction is given in Figure 1.18. The lead from the electrode to the device is driven with small impedance increasing noise immunity. Because of the capacitive structure only AC signals can be measured. The high input impedance assures quite low corner frequency: 0.005 Hz (-3 dB) can be reached.

Figure 1.18. Structure of an active electrode



Needle electrodes

Surface electrodes can measure only the integral of the electrical activity inside the human body. Needle electrodes can access inner parts: activity in muscles (EMG) or in the brain (EEG). In the tip of the needle several electrodes can be built in [1.3], see Figure 1.19.

Figure 1.19. Matrix arrangement of electrodes for measuring brain activity (Neuronelektrod Kft.) http://www.neuronelektrod.hu/getpage.php?oldal_id=351

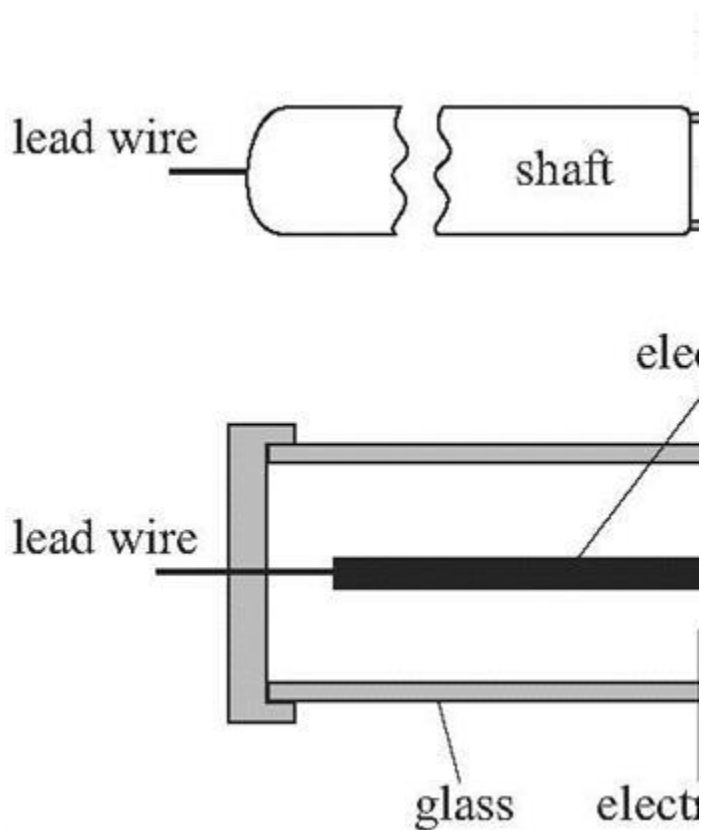


Special solutions

For astronauts NASA developed spray-on electrodes in the 1960's. A fast drying conductive mixture was applied to wires. The disadvantage is that the natural breathing of skin is blocked. This electrode type has not become widely used.

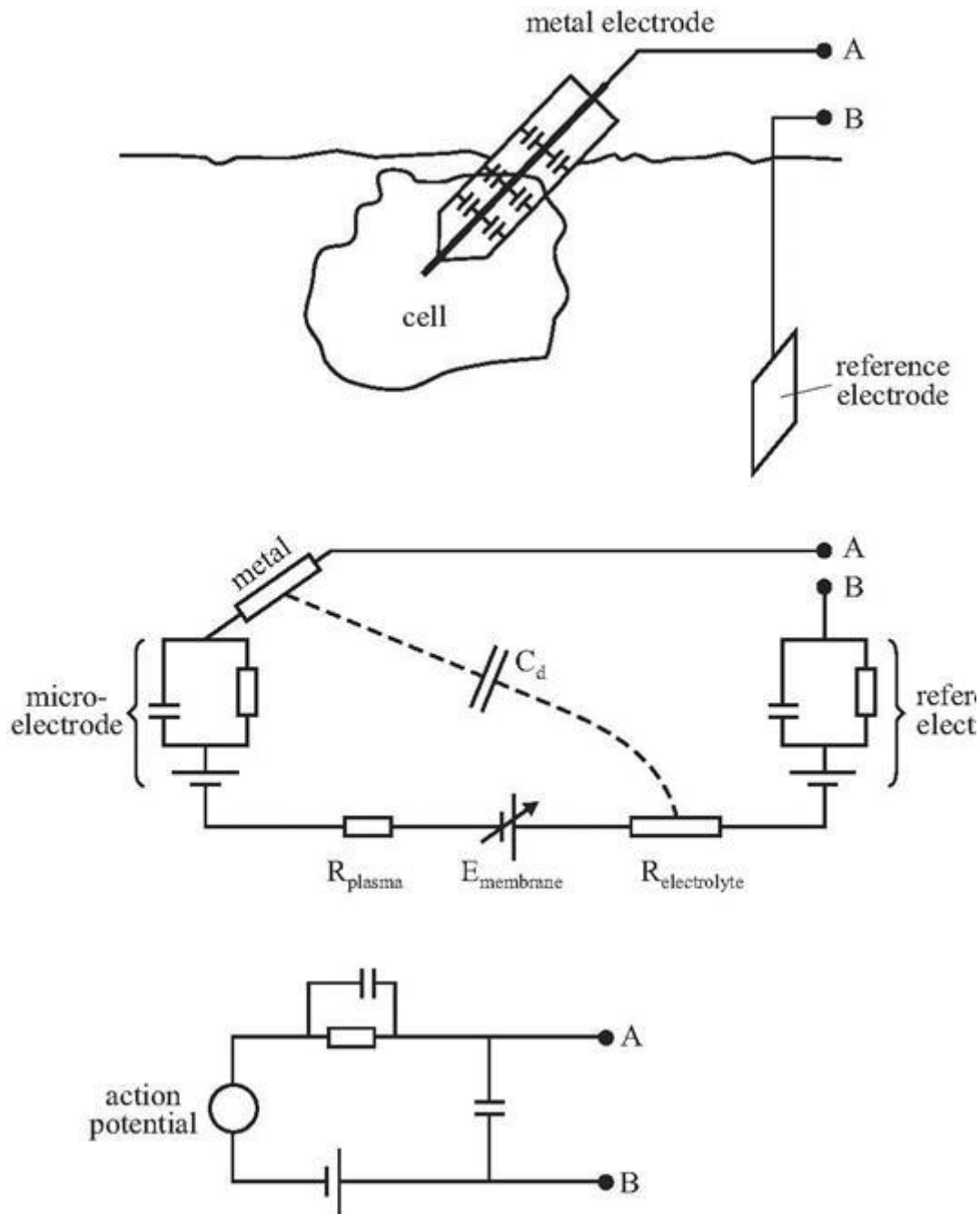
9. Microelectrodes

Figure 1.20. Glass (below) and metal (above) microelectrode structure



Mainly during in-vitro research the electrical activity of a single cell is needed. It requires access to the inner part of a cell. The tip of such a microelectrode must have a very small diameter ($0.05 \dots 10 \mu\text{m}$) though solid enough to penetrate the membrane. Figure 1.20 shows the structure of the two basic microelectrode types, metal and glass. One possible model of the measurement with a metal microelectrode is given in Figure 1.21.

Figure 1.21. Model of metal microelectrode



The stem of a metal microelectrode must be insulated (see Figure 1.20). There are conductors on both sides of the insulation. The structure forms a capacitance, its value can be estimated by eq. 1.19.

$$C_d = L \frac{2\pi\epsilon_r\epsilon_0}{\ln\left(\frac{D}{d}\right)} \quad (1.19)$$

where C_d is the resultant of stray capacitances, the permittivity of vacuum is ϵ_0 that of insulation is ϵ_r , the outer diameter of the stem is D , the inner one is d , and L is the length of the stem.

The glass microelectrode is filled with electrolyte; its impedance depends on the shape. If the shape is cylindrical then $R_{ei} = \rho l/A$, if cone-shaped then $R_{ei} = 4\rho/(\pi\Phi d)$ gives a good estimate (ρ is the resistivity, l is the length of the cylindrical part, A is the cross section of the cylindrical part, d is the diameter of the electrode tip and Φ is the cone angle).

Because of the very small size, at the tip of microelectrodes we have to take into account the spreading resistance. It can be estimated as $R_{sp} = \rho_e/2(4\pi d)$ (ρ_e is the resistivity of the electrolyte the electrode is immersed

into, d is the diameter of the tip). The usual value for R_{el} for glass electrodes is 30 ... 500 M Ω . For both glass and metal microelectrodes R_{sp} is cca. 1 M Ω , C_{el} 1 ... 5 pF. The transfer function of microelectrodes is low-pass type, the corner frequency is a few kHz.

10. Problems

1. The thickness of a cell membrane is 11 nm, its relative permittivity is 12.6. Calculate the capacitance per unit area of the membrane. ($\epsilon_0 = 8.85 \times 10^{-12}$ As/Vm) Calculate the capacitance of a membrane with a membrane area of 4×10^{-12} m².
2. The permeability of an ion-selective (K^+ selective) membrane to different ions:

$$P_{Na} = 10^{-7} \text{ cm/s}, P_K = 3 \times 10^{-4} \text{ cm/s}, P_{Cl} = 5 \times 10^{-7} \text{ cm/s}.$$

The ion concentrations on the two sides of the membrane:

	chamber 1	chamber 2
K	unknown	60mM
Na	20mM	40mM
Cl	100mM	300mM

The potential difference across the membrane is: 16mV. (ΔU calculated according to eq. 1.16).

Calculate the K concentration in chamber 1.

3. During action potential the inner part of the squid axon changes its potential relative to the external part from -70 mV to +20 mV.

The capacitance per unit area of the membrane is 1 μ F/cm². Calculate the charge passing through the membrane, provided the ion flux is evenly distributed along the membrane area.

(Faraday's constant is 96500C/mol.)

4. Calculate the charge flowing through the membrane of a disc-shaped cell (diameter: 20 μ m, height: 5 μ m), if the capacitance per unit area and the potential change is the same as given in problem 3.
5. Calculate the percentage of the charge flowing into the cell according to problem 3 and the charge being there before the action potential. The concentration of the solution in the cell before the action potential is 0.3 mol/l.
6. Calculate the percentage of the charge flowing into the cell according to problem 4 and the charge being there before the action potential. The concentration of the solution in the cell before the action potential is 0.4 mol/l.
7. The potential across a cell membrane is -80 mV, the thickness of the membrane is 10 nm. Calculate the electric field across the membrane.
8. The ion concentrations below are measured inside and outside of a cell:

ion	internal	external	permeability, cm/s
K^+	155mM	4mM	2×10^{-6}
Na^+	12mM	145mM	2×10^{-8}

Cl ⁻	4mM	120mM	4x10 ⁻⁶
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$R = 8.31 \text{ J/(mol} \cdot \text{K)}$, $F = 96500 \text{ C/mol}$. Calculate the potential across the membrane ($T = 293 \text{ }^\circ\text{K}$).

9. There is KCl in two chambers separated by a membrane. The concentration of KCl is different in the chambers. The membrane is permeable only to K⁺ ions. At $T = 298 \text{ }^\circ\text{K}$ we measure 10 mV potential difference across the membrane. Give the ratio of K⁺ ion concentrations in the two chambers.
10. We have the same chambers as in problem 9 and measure the same potential difference. The concentration of KCl in chamber 1 is 0.1 mol/l. Give the possible range of KCl concentration in chamber 2, provided we can measure temperature with $\pm 1^\circ\text{K}$ uncertainty.
11. The permeability of an ion-selective (Na⁺ selective) membrane to different ions:

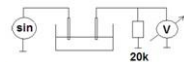
$$P_{\text{Na}} = 2 \times 10^{-4} \text{ cm/s}, P_{\text{K}} = 10^{-6} \text{ cm/s}, P_{\text{Cl}} = 5 \times 10^{-7} \text{ cm/s}.$$

The membrane separates two chambers where the ion concentrations are:

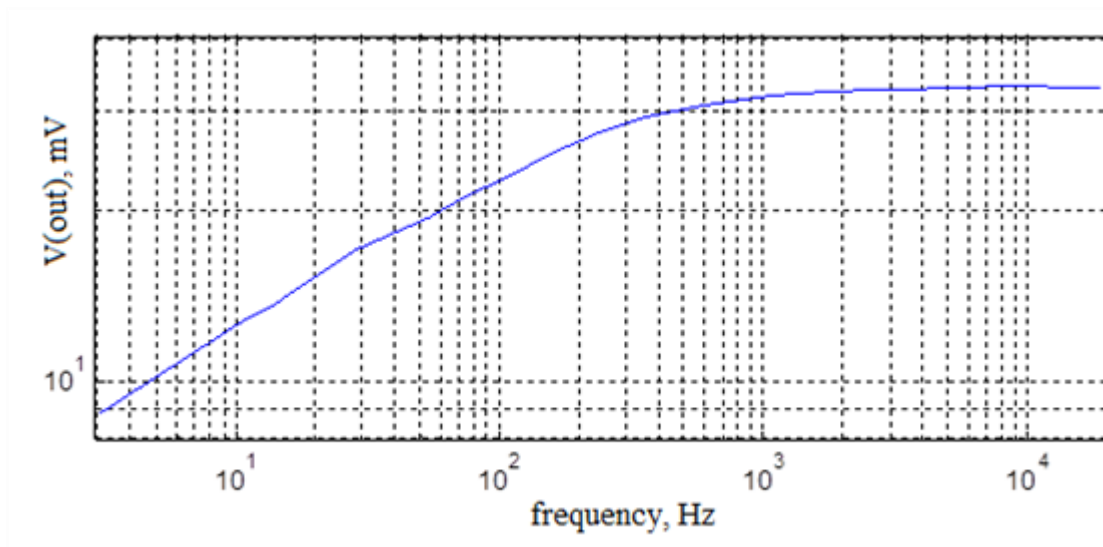
	chamber 1	chamber 2
K ⁺	20mM	400mM
Na ⁺	20mM	40mM
Cl ⁻	100mM	50mM

Calculate the potential difference between the two chambers.

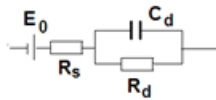
12. Calculate the difference in potential between the two chambers if the Na concentration in chamber 1 increases by 20%.
13. Calculate the difference in potential between the two chambers if the K concentration in chamber 1 increases by 20%.
14. Two identical Ag/AgCl electrodes are tested as given in Figure 1.22.



The amplitude of the sine wave is 34.1 mV. Ideal voltmeter V reads the values given in Figure 1.23 as the frequency of generator $\sin$ varies from 0.1 Hz to 10^4 Hz.



On 10 kHz the amplitude of the output voltage is 32.9mV. Estimate the serial resistance of electrodes supposing the model given in Figure 1.24.



15. In two chambers separated by a membrane there is urea (carbamide). The concentration in chamber 1 is 20 mmol/l, in chamber 2 60 mmol/l. The permeability of the membrane to urea is 2×10^{-6} cm/s. Calculate the diffusion flux.

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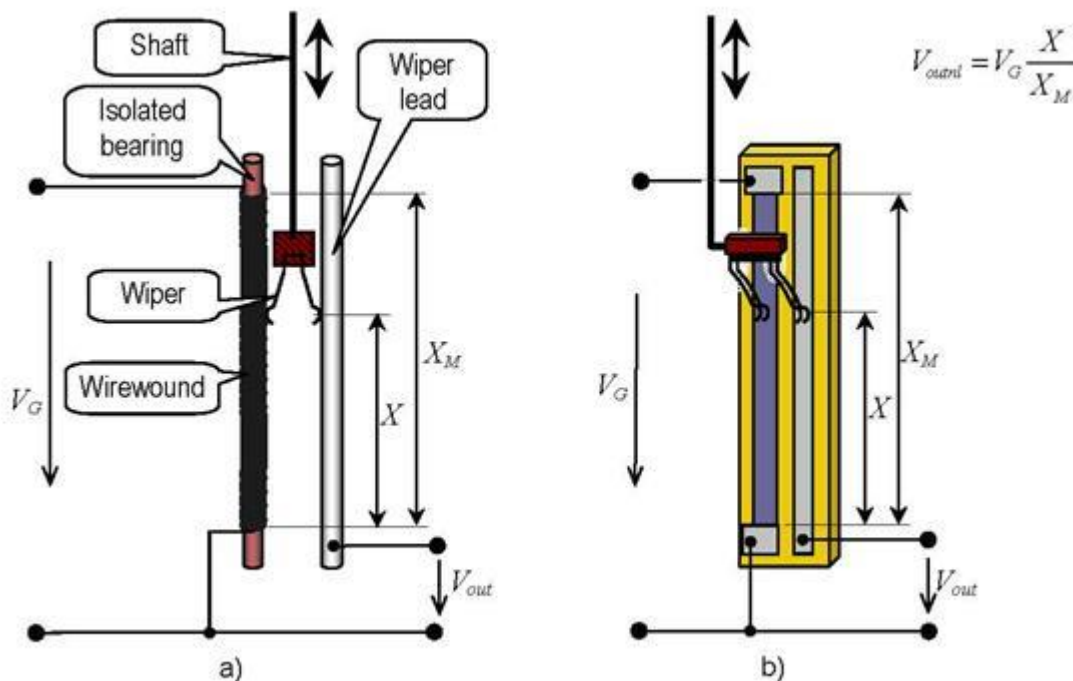
Chapter 2. Biomedical sensors and transducers

Non-electrical quantities are usually measured by first converting them into electrical signal. Following primary processing (amplification, noise suppression, signal conditioning) the analogue signal is digitised. Further signal processing is done by computers. This chapter deals with the basic principles of sensors and transducers.

1. Measurement of mechanical quantities

1.1. Potentiometers

Figure 2.1. Converting linear displacement into voltage using wire wound (a) and film (carbon or cermet) potentiometer (b)

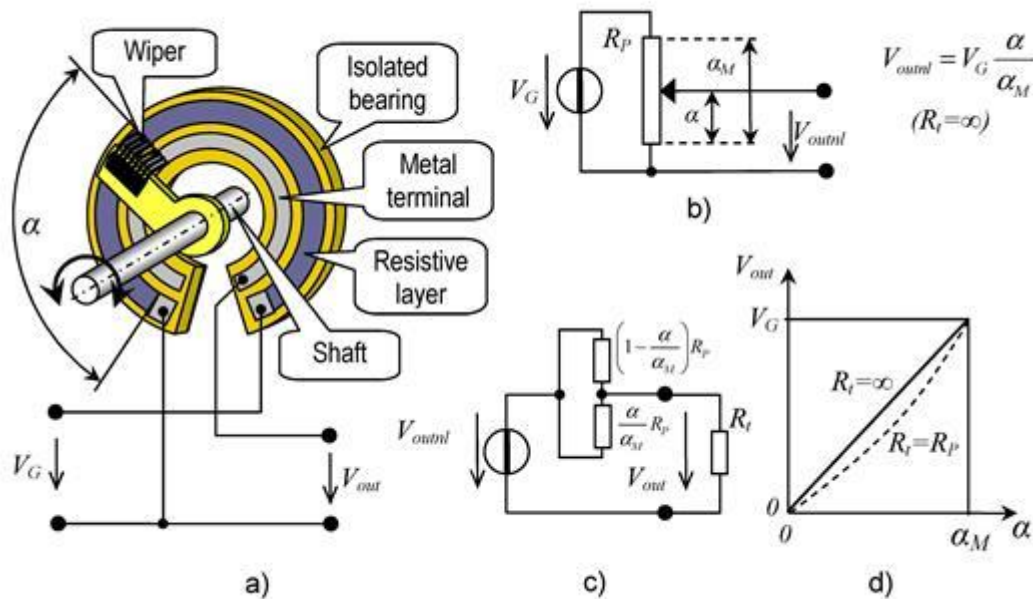


10 – 100 mm linear displacement and rotation (large) can easily be converted into electrical signal using potentiometers (Figure 2.1.). These are used as voltage dividers. The displacement or rotation to be measured moves the taper (wiper) and as a result the output voltage changes. If the input voltage is constant then the output voltage is proportional to displacement or rotation to be measured. Using mechanical transmission the range of the transducer can be increased, decreased (to increase sensitivity), the orientation can be inverted. Figure 2.2.a shows a typical sensor set-up. The no load voltage is proportional to displacement (rotation) but the output resultant resistance of the potentiometer also depends on displacement (rotation), see Figure 2.2 c and d. The required load resistance is much greater than the R_p resistance of the potentiometer.

Disadvantage of this simple and cheap solution is that both the taper and the carbon (cermet) wear out during usage, requires maintenance, the moving wiper induces electrical noise. These disadvantages can be avoided by using other kind of transducers (e.g. inductive ones).

Potentiometers are available in the $10\ \Omega$ – $10\ \text{M}\Omega$ range. Potentiometers used as transducers are usually in the $1\ \text{k}\Omega$ – $100\ \text{k}\Omega$ range.

Figure 2.2. The rotary potentiometer used as a sensor. The structure (a), symbol (b), model to calculate the loaded characteristics (c), and the transfer characteristics (d).



1.2. Strain gauges

The resistance of a conductor with length l , cross section A and resistivity ρ is:

$$R = \rho \frac{l}{A} \quad (2.1)$$

If the relative changes of the parameters of the strain gauge are small then the relative change of the resistance can be approximated by eq. 2.2.

$$\frac{\Delta R}{R} \cong \frac{\Delta \rho}{\rho} + \frac{\Delta l}{l} - \frac{\Delta A}{A} \quad (2.2)$$

Stretching the conductor within its limits of elasticity its cross section decreases (see Figure 2.3.a). Supposing the volume of the conductor remains constant, the change relation of the changes:

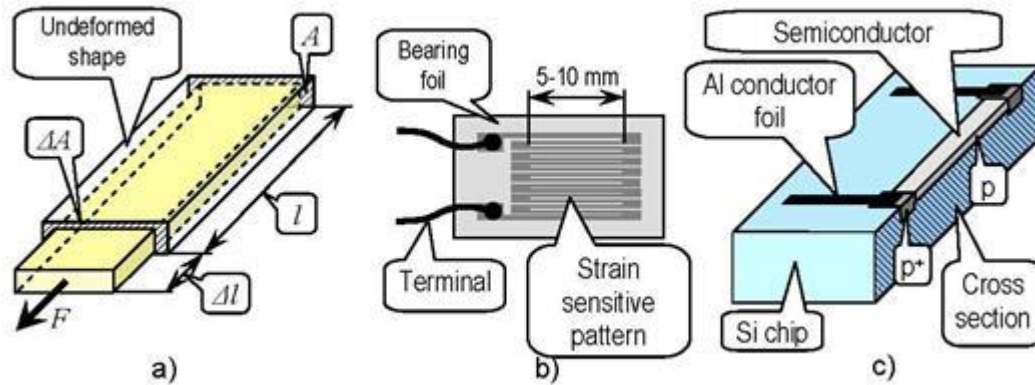
$$\frac{\Delta A}{A} = -\frac{\Delta l}{l} \quad (2.3)$$

Taking it into account:

$$\frac{\Delta R}{R} \cong \frac{\Delta \rho}{\rho} + 2\frac{\Delta l}{l} \quad (2.4)$$

Typical strain gauge structure [2.4] is shown in Figure 2.3.b. A long, thin conductive strip is formed – formerly bonded, nowadays rather deposited on an insulating layer – in a meander pattern of parallel lines. The sensitivity of the meander (zig-zag) form is much higher in the direction of the parallel lines. The force or bending to be measured determines the $\Delta l/l$ relative extension.

Figure 2.3. Strain gauges. Deformation of metal wire as a result of stretch (a). Strain gauge foil (b) and semiconductor strain gauge or piezoresistor (c).



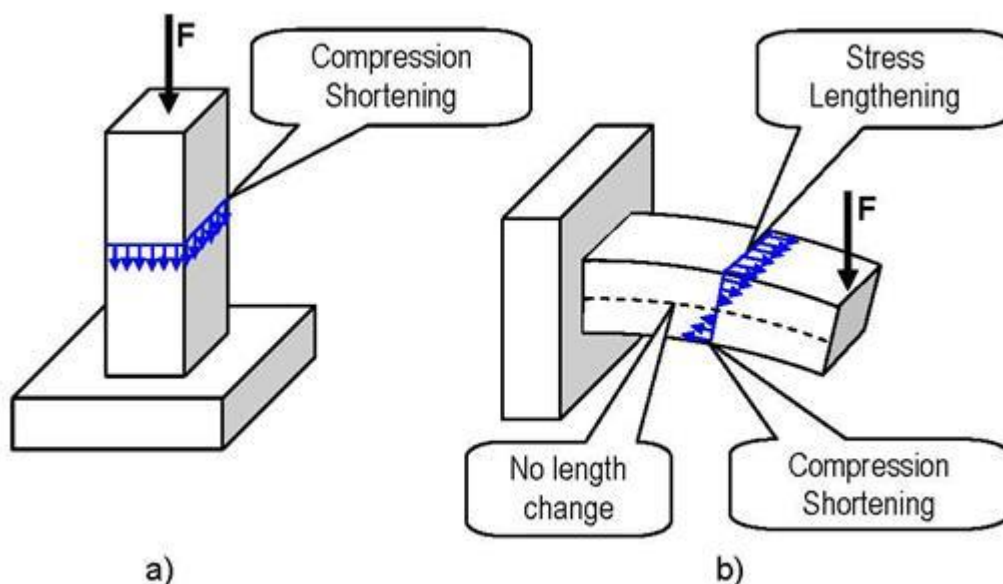
The semiconductor strain gauge (also called piezoresistor, see Figure 2.3. c) has higher sensitivity, but it is more expensive, its temperature coefficient is higher and it is more fragile. The characteristic parameters of strain gauges are: nominal resistance R , the gauge factor G and the temperature coefficient TK (see eq. 2.5 and 2.6).

$$G = \frac{\frac{\Delta R}{R}}{\frac{\Delta l}{l}} \quad (2.5)$$

$$TK = \frac{\frac{\Delta R}{R}}{\Delta T} \quad (2.6)$$

Table 2.1 gives the parameters of metal and semiconductor strain gauges. The resistivity of metal strain gauges does not change during stress ($\Delta\rho \approx 0$). As a result, their gauge factor is close to 2. The resistivity of semiconductor strain gauges changes significantly during stress ($\Delta\rho/\rho \gg l$). This is called piezoresistive effect.

Figure 2.4. Deformations to be measured (exaggerated). Deformation of a stressed or compressed object has similar deformation on each side (a). Bending of the object results in both stress and compression at the same time (b).



Semiconductor strain gauges are typically manufactured using semiconductor technology. The resulting element is small; often the necessary amplifiers are also integrated. Complete pressure- and acceleration sensors are available.

Strain gauges are usually attached to objects. Figure 2.4 shows the deformation and the related forces when the object is stressed, compressed or bent.

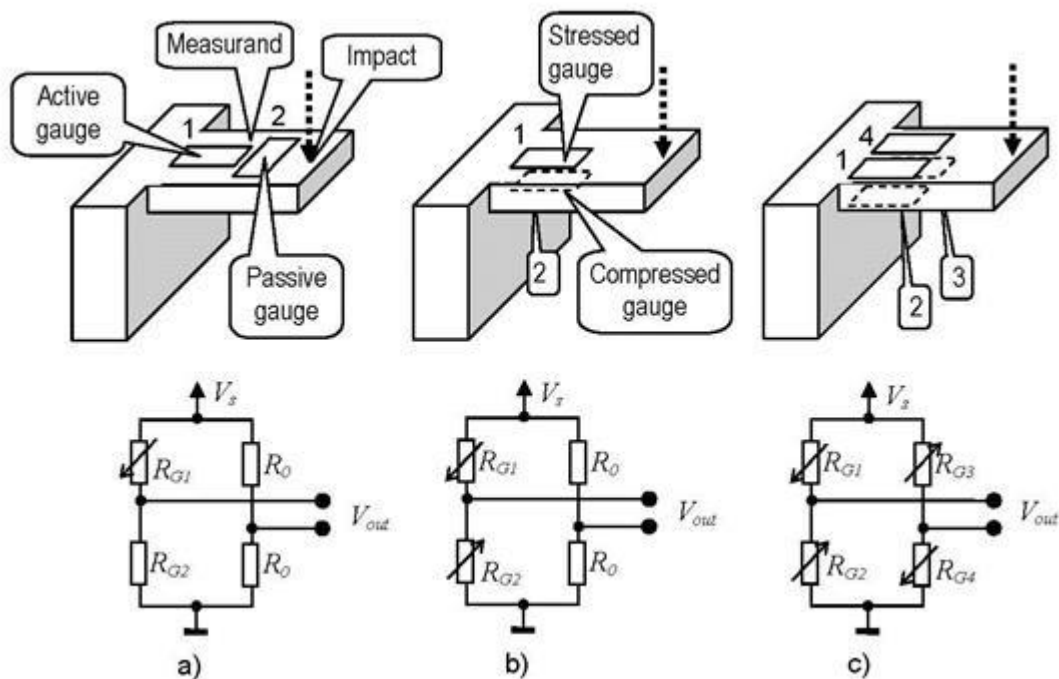
Table 2.1. Parameters of strain gauges

Material	Composition	R	G	TK
Constantan	Ni 45%, Cu 55%	80 – 1000 Ω	2 – 2.1	± 20 ppm/ $^{\circ}\text{C}$
Nichrome V	Ni 80%, Cr 20%	80 – 1000 Ω	2.1 – 2.6	100 ppm/ $^{\circ}\text{C}$
Si crystal	p-type contamination	1-5 k Ω	100 ... 170	700 – 7000 ppm/ $^{\circ}\text{C}$
Si crystal	n-type contamination	1-5 k Ω	-50 ... -120	700 – 7000 ppm/ $^{\circ}\text{C}$

1.3. Measurement circuits for strain gauges

Measurement circuits for strain gauges are detailed in [2.5]. The dilatation of the object caused by temperature change influences also the strain gauge. Furthermore, temperature change also influences the resistivity (ρ) of the foil. This is characterised by the temperature coefficient, TK. These errors are not negligible compared to the deformation to be measured. Measurement with a single strain gauge is only possible if the temperature coefficient compensates the dilatation ($\text{TK} < 0$). Errors caused by temperature change can be eliminated by detecting the resistance difference of two strain gauges. One strain gauge should be fixed so that its sensitive direction is in line with the deformation while the other perpendicularly to it. This latter is called passive strain gauge. The two strain gauges form a voltage divider, and the divided voltage is the output signal depending on the deformation. Figure 2.5.a shows possible configuration of active and passive strain gauges and the corresponding measuring circuitry. If the output voltage is measured then the necessary measurement range is about $V_s/2$, while the voltage change resulting from the deformation is much smaller: $\Delta V/V_s < 1\%$. The solution is to augment the circuitry by two resistors R_0 with equal value and small TK. The resulting structure is called a bridge; its output voltage can be amplified with a symmetrical amplifier. (Symmetrical amplifiers are detailed in Chapter 3.)

Figure 2.5. Force measurement with one active and one passive strain gauge (a), with two active strain gauges (b), and with four active strain gauges (c)



When two active strain gauges are applied (one exposed to opposing deformation, see Figure 2.5. b) then the sensitivity is doubled and temperature dependence is compensated. The best solution is to apply four active strain gauges (see Figure 2.5.c). The strain gauges diagonally in the bridge are exposed to the same deformation.

Sensitivity of a four active strain gauge bridge is four times higher than with one active strain gauge. The simplest measuring devices use $V_s = 3 \dots 6$ V DC as the supply voltage of the bridge. In precision measurement devices the supply voltage is $f_s = 4 \dots 20$ kHz frequency AC voltage to eliminate the contact potentials. The nominal (unloaded) resistance of strain gauges is within a few percentages. Even so the output voltage of the unloaded bridge circuit can be too high, so compensation is necessary. Furthermore, there must be a way to zero the output voltage before starting the measurement. The own weight of the measuring object needs zeroing, as the sensor can be applied in different positions. Figure 2.32 shows possible solutions.

1.4. Pressure sensors

Pressure measurement is nearly always based on the deformation of a membrane [2.6]. The deformation of the membrane can be converted into electrical signal using strain gauges. Small membranes can be manufactured together with the necessary elements as an integrated circuit. Manufacturing requires that the stressed and compressed strain gauges be on the same side of the membrane. This is illustrated in Figure 2.6.b. While deformation is small, resistivity change is nearly proportional to the pressure difference between the two sides. When the pressure difference is greater linearization is necessary. This is done by the signal processing circuitry, most often also integrated on the chip.

Figure 2.6. Pressure sensor formed on a silicon crystal. The cross section of the chip (a), the view of the arrangement (b) and the deformation of the membrane blown up (c).

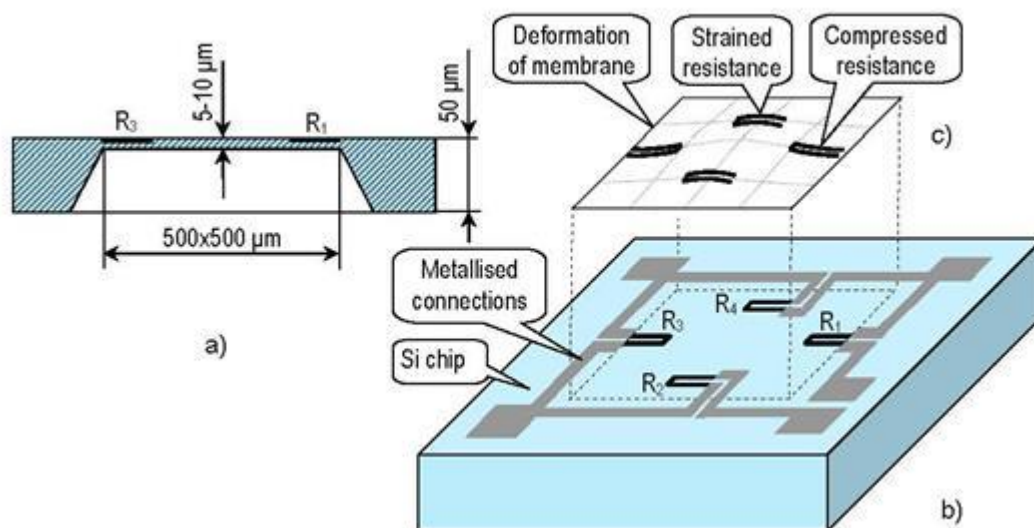
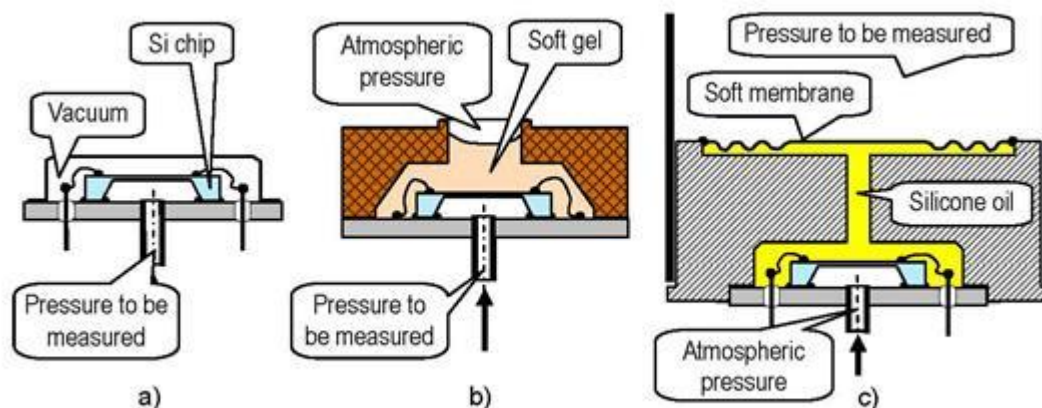


Figure 2.7. Pressure sensors formed using semiconductor chips. Measuring absolute pressure (a), differential pressure (b, c). In (c) the pressure is conveyed by oil.



Silicon membrane becomes pressure sensor as a result of packaging. Figure 2.7 shows three typical solutions. The chamber formed on one side of the membrane is in connection with the pressure to be measured. The medium gets into the chamber directly (when measuring gas pressure) or by an intermediate liquid. In this latter case a second membrane is usually applied between the intermediate liquid and the one to be measured. On the other side of the sensor membrane is vacuum; if the absolute pressure should be measured. If differential pressure is to be measured, then the pressures should be present at the two sides of the sensor membrane.

Characteristic parameters of piezoresistive sensors:

Usual supply: 3-10 V, or 1-2mA. $R_{\text{bridge}} = 1-5 \text{ k}\Omega$

Sensitivity: $\Delta V_{\text{out}}/V_s = 1-10 \text{ mV/V}$ at nominal pressure.

Corner frequency: 1-2 kHz

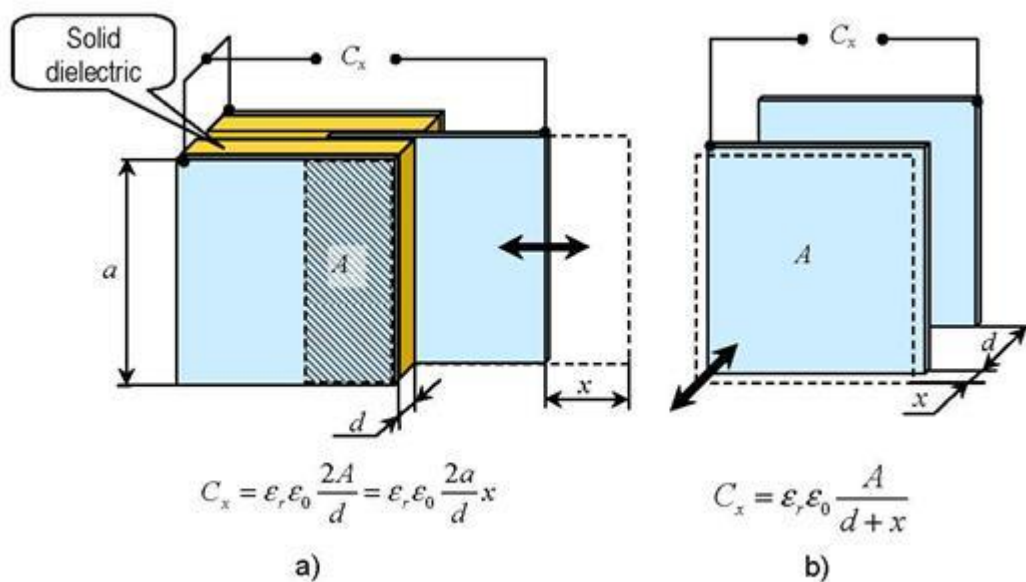
1.5. Capacitive sensors

The capacitance of a planar capacitor depends on the size and the dielectric used:

$$C = \epsilon_r \epsilon_0 \frac{A}{d} \quad (2.7)$$

where $\epsilon_0 = 8.85 \times 10^{-12} \text{ As/Vm}$, is the permittivity of vacuum, ϵ_r is the relative (to vacuum) permittivity of the dielectric (dimensionless). The displacement to be measured changes the position of plate(s). As a result, the effective area changes, see Figure 2.8.a. The arrangement shown has linear characteristics. Other shape of the plate can result in other characteristics (disc section shape is used in rotation – capacitance transducers).

Figure 2.8. Possible schemes of capacitive displacement transducers. When the effective area is changed solid dielectric can be applied (a). When the distance between plates is changed the dielectric is air (b).



Small displacement can be measured by changing the distance between plates. However, the $C_x=f(x)$ characteristics will be non-linear.

A differential capacitance not only eliminates nonlinearity, but it can be manufactured easier (see Figure 2.9.a). Two capacitances are formed by three plates. The two terminal plates are fixed. The plate in between (common plate) is moving in proportion to the displacement to be measured. As the plate moves one capacitance gets

smaller and the other greater. Measuring the two capacitances using a bridge we get an output voltage proportional to the displacement:

$$V_x = 2V_0 \frac{X_{c1}}{X_{c1} + X_{c2}} - V_0 \quad (2.8)$$

The two capacitances:

$$C_1 = \epsilon_r \epsilon_0 \frac{A}{d_0 + x} \quad (2.9)$$

and

$$C_2 = \epsilon_r \epsilon_0 \frac{A}{d_0 - x} \quad (2.10)$$

The reactance of the two capacitors:

$$X_{c1} = \frac{1}{\omega C_1} = \frac{d_0 + x}{\omega \epsilon_r \epsilon_0 A} \quad (2.11)$$

and

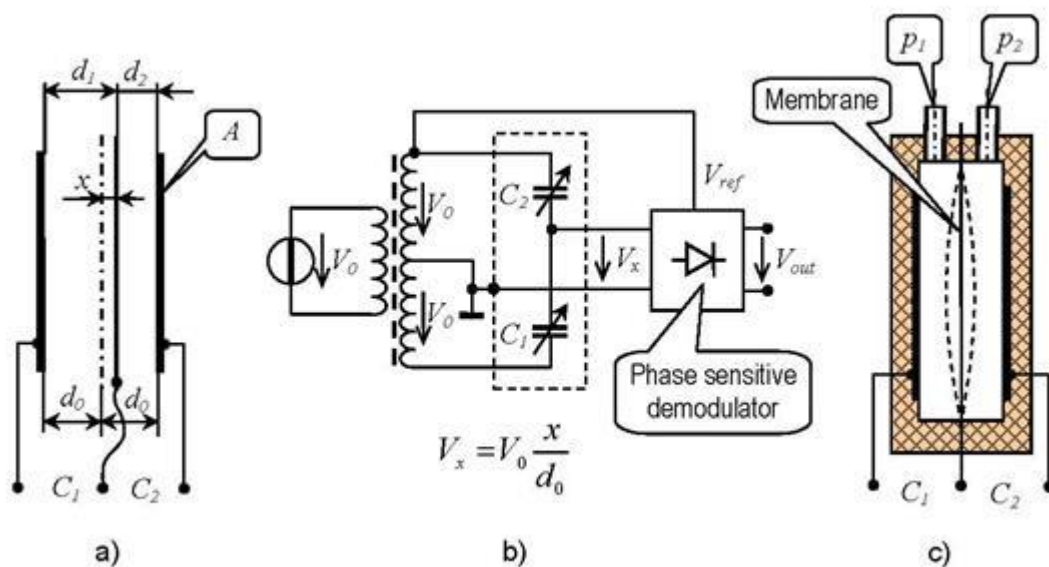
$$X_{c2} = \frac{1}{\omega C_2} = \frac{d_0 - x}{\omega \epsilon_r \epsilon_0 A} \quad (2.12)$$

Taking these into account the output voltage of the bridge is:

$$V_x = 2V_0 \frac{d_0 + x}{2d_0} - V_0 = U_0 \left(\frac{d_0 + x}{d_0} - 1 \right) = V_0 \frac{x}{d_0} \quad (2.13)$$

The application of a differential capacitance not only linearises the output voltage – displacement characteristics, but also eliminates the effect of ϵ_r as a source of error.

Figure 2.9. Model of the displacement transducer based on differential capacitance (a), measurement circuitry resulting in linear transfer characteristics (b), applying the differential capacitance principle in a differential pressure sensor (c)



Using 10 – 100 kHz supply voltage and phase-sensitive demodulation the value of the output voltage is proportional to the displacement and the sign of the output voltage shows the direction of the displacement. If the common plate moves as indicated in Figure 2.9.a, the $C_2 > C_1$ and V_x is in phase with V_{ref} . Typical application is the pressure difference sensor; its principle of operation is given in Figure 2.9.c. The pressure difference deforms the membrane, the change in capacitances C_1 and C_2 can be measured the same way as given in Figure 2.9.b. It must be taken into account that the dielectric is the medium to be measured.

1.6. Inductive position sensors

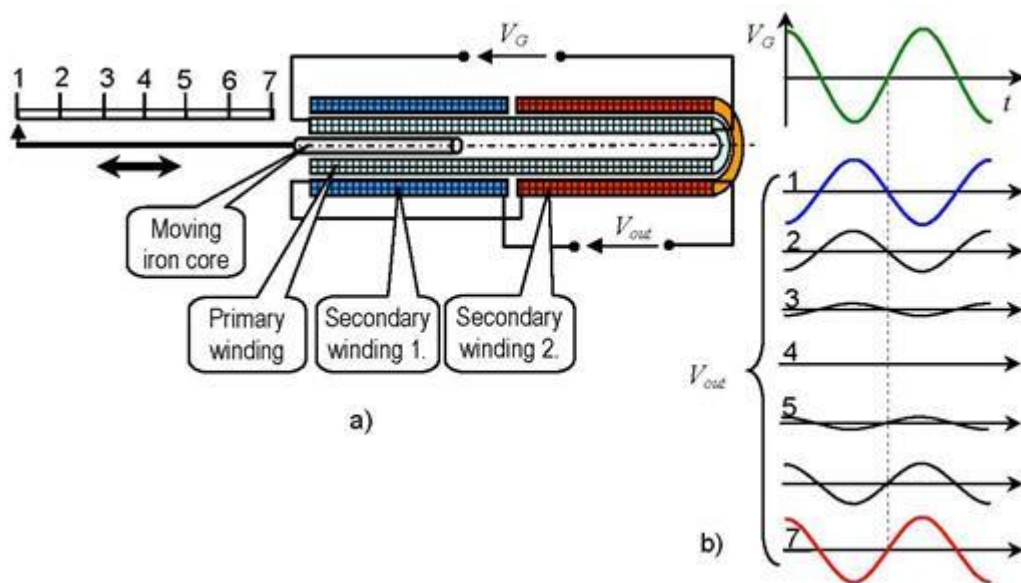
Displacement can be converted into change of inductance using two serial solenoids. Displacement or rotation can change the relative position of the two solenoids. The displacement of the core also changes the inductance of a coil [2.7], [2.8]. A circuitry is needed that converts the change of inductance to voltage proportional to displacement (or rotation). This is usually done by comparing the changing inductivity to a fix one. Linear Voltage Differential Transformers (LVDT) are available with various measurement ranges: from 0 – 2 mm to 0 – 500 mm. LVDTs have small nonlinearity error, 0.5% within the whole measurement range is typical.

Typical set-up is given in Figure 2.10.a. The excitation signal (constant amplitude 2 – 10 V, and frequency 2 – 10 kHz) is applied to the internal solenoid. Without a core the voltages induced in the two external solenoids cancel each other, the resulting output voltage is zero. As the core moves the coupling between the internal and the two external solenoids changes. The output voltage corresponding to different core positions is given in Figure 2.10.b.

The output voltage produced by the phase-sensitive demodulator is DC. The sign of the DC output voltage indicates the direction of the displacement of the core from null-position (marked by 4 in Figure 2.10.a). The transducers offered by different manufacturers can use different solenoid arrangement, but the theory of operation is the same.

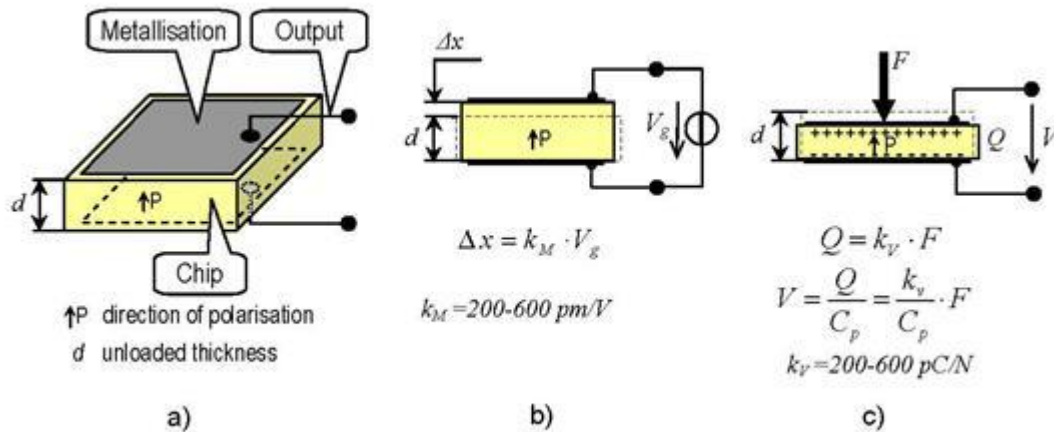
Further important parameters of inductive position sensors are: friction, moving mass, maximal velocity, wearing out, and construction without sliding contact.

Figure 2.10. Linear Voltage Differential Transformer (LVDT): theory of operation (a) and output voltage belonging to different core positions (b)



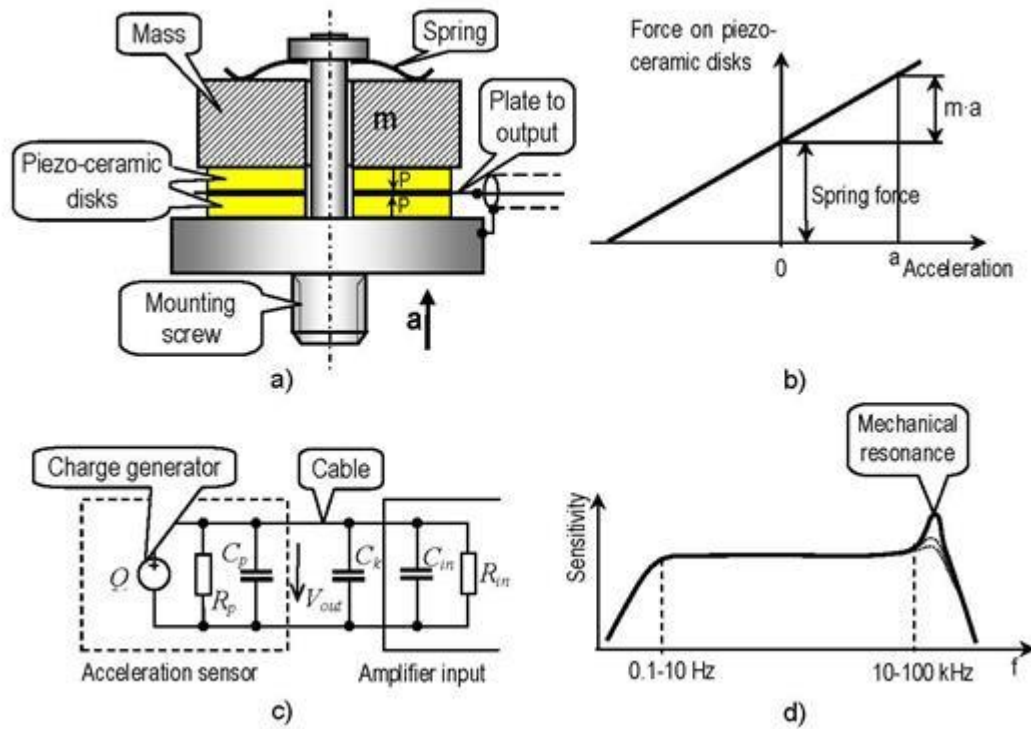
1.7. Piezoelectric sensors

Figure 2.11. Piezoelectric sensor: build-up (a), operation as electric – mechanical (b) and mechanical – electric (c) converter



Piezoelectricity is the property of certain materials (crystal, some ceramics, bone, even some proteins) to accumulate charge in response to mechanical stress or vice versa. Depending on how the piezoelectric material is cut the sensor can have three modes of operation: transverse, longitudinal and shear. The two opposite surfaces of the sensor are metalized ensuring electrical contact. Applying voltage to the two opposite metal contact changes the thickness of the sensor. Applying force on the sensor generates electrical charge that develops voltage V across the C_p capacitance of the sensor. The piezoelectric sensor can be used as electric – mechanical or as mechanical – electric transducer [2.9] (see Figure 2.11). The natural piezoelectric property of quartz crystal is used mainly as an element to assure stable frequency of oscillators. Piezoelectric sensors and transducers are fabricated from polycrystalline ceramics, most often from lead zirconate titanate (PZT). Polymer based sensors (polyvinylidene difluoride, PVDF) are also used. Ceramic and polymer sensors can be fabricated to arbitrary shape. Piezoelectric property is formed using high DC voltage. (These materials are also called ferroelectric materials referring to the analogy with magnetic materials.) The direction of polarizing voltage determines the polarity of the output voltage caused by a given stress direction.

Figure 2.12. Build-up of a piezoelectric acceleration sensor (a), the role of the spring force (b), electrical model of measurement (c) and the typical frequency dependence of the sensor (d)



In piezoceramic materials piezoelectric effect is much stronger than in quartz crystals. Piezoelectric sensors can measure force as shown in Figure 2.11.c. Contrary to strain gauges, static force cannot be measured, because the leakage current due to resistances (see Figure 2.12) decreases the charge.

During vibration measurement acceleration sensors convert variable force into electrical signal [2.10]. Figure 2.12.a shows the cross section of an acceleration sensor. The sensor is made up of two piezoceramic disks restrained by a spring, and a seismic mass. As a result of its inertia the mass exerts force on the disks during vertical acceleration of the sensor. Application of two disks increases the output signal and offers easy connection of insulated lead wires. The compression with a spring makes possible the measurement of downward acceleration (in Figure 2.12.a negative acceleration). Negative acceleration decreases the compressing force resulting in a charge with opposite sign compared to upward (positive) acceleration.

The restraining force changes during acceleration a :

$$\Delta F = ma \quad (2.14)$$

The emerging piezoelectric charge is:

$$Q = k_v \Delta F \quad (2.15)$$

The charge generates the output voltage across the resultant capacitance:

$$V_{out} = \frac{Q}{C_p + C_c + C_{in}} = \frac{k_v m}{C_p + C_c + C_{in}} a \quad (2.16)$$

The capacitance of the piezoelectric plate C_p is given, the capacitance of the cable and the input capacitance of the amplifier must be kept as low as possible to minimize the attenuation of the output voltage of the sensor. Often an amplifier separates the output of the sensor from the capacitive load; thus sensitivity of the sensor remains constant even if cable capacitance changes. Another possible solution is to connect a charge amplifier to the output of the sensor. The charge amplifier has nearly zero input impedance, it takes the whole generated charge thus capacitances do not load [2.11], [2.12], [2.13].

Typical sensitivity is: 0.1-10 mV/ms². The sensitivity of the sensor is constant over a broad frequency range (see Figure 2.12.d). The low-frequency corner frequency is determined by the R and C elements of the electrical model:

$$f_{\text{low}} = \frac{1}{2\pi R_e C_e} \quad (2.17)$$

where $R_e = R_p \times R_{in}$, and $C_e = C_p + C_c + C_{in}$.

The high-frequency corner frequency is limited by the mechanical resonance, determined by the seismic mass and the elasticity of the piezoceramic disks.

Piezoelectric acceleration sensor perceives only changes in acceleration, neglects the constant acceleration due to gravity. However, rotation changes the projection of gravitational acceleration on the direction of the shaft of the sensor thus generating output voltage. Calculating the displacement and rotation of an acceleration sensor based on its output signal is an inverse problem. Different movements cause the same output signal. A priori information about the movement helps process the output signal of an acceleration sensor.

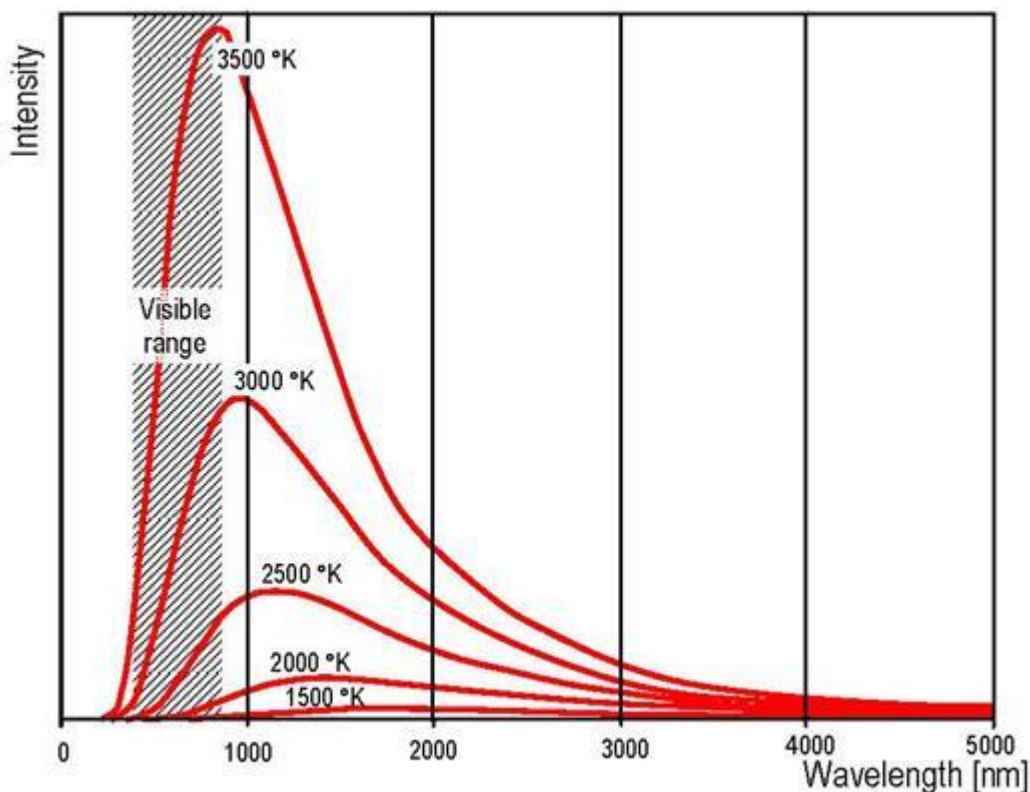
Another application of piezoelectric transducers is generation and detection of ultrasound. This is detailed in section 2.3. The need for mini (even micro) displacement transducers and motors is increasing, also in surgery.

2. Photoelectric transducers

Light absorption of a biological samples and organs gives diagnostic information. The frequency of the light used should be selected depending on the sample to be measured. The necessary frequency determines the appropriate light source and detector.

2.1. Light sources

Figure 2.13. Black-body radiation as a function of temperature



Light absorption measurements of biological samples are performed with frequencies from ultraviolet (UV) to infrared (IR). The visible light (VIS) is within this frequency range.

Testing human vision the *sensation* of light has to be assessed. For measurements not related to human vision the emitted light is characterized by the frequency range and the *power* (W) over this frequency range. This duality has to be taken into account when defining the units of light (optical) radiation.

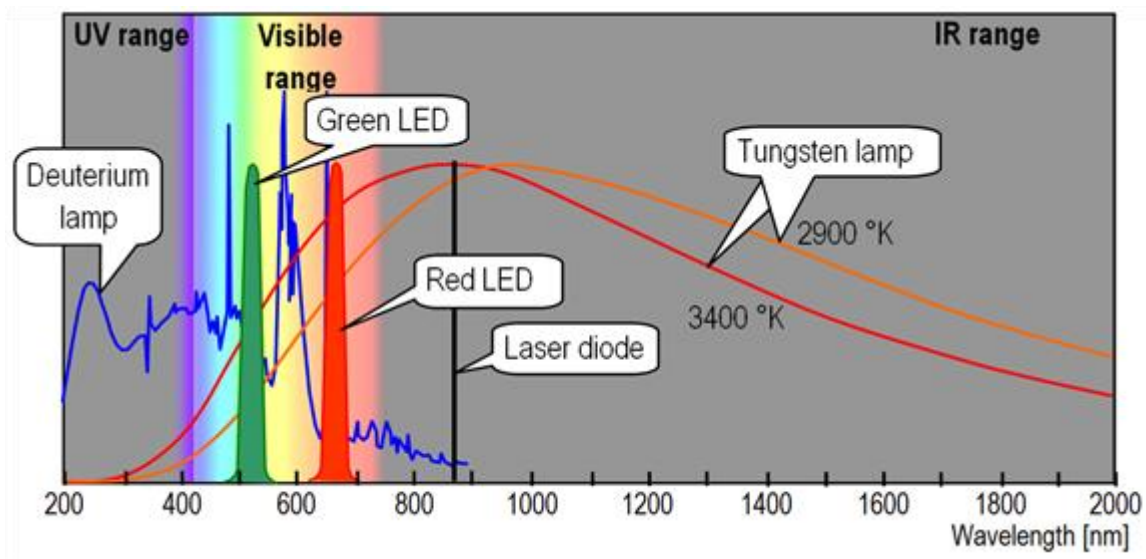
Radiation of metals has continuous frequency spectrum. The distribution of radiated energy over frequency depends on the temperature of the metal. The frequency distribution of black-body radiation at different temperatures is given in Figure 2.13. The intensity of radiation at a given wavelength is given by Planck's law, see eq. 2.18.

$$W_{\lambda b} = \frac{2\pi c^2 h}{\lambda^5 (e^{(hc/k\lambda T)} - 1)} \quad (2.18)$$

where $W_{\lambda b}$ is the power of radiation on wavelength λ , T is the temperature of the black-body, c is velocity of light, $h = 6.626 \times 10^{-34}$ Js is Planck constant, $k = 1.38 \times 10^{-23}$ J/K is Boltzmann constant.

Figure 2.13 shows that as the temperature increases the intensity of radiation strongly increases, the dominance of the peak increases and the peak intensity shifts to lower wavelength. At around 6000 °K the peak of the spectrum is in the middle of visible frequency range. Figure 2.14 shows the spectrum of some frequently used light source.

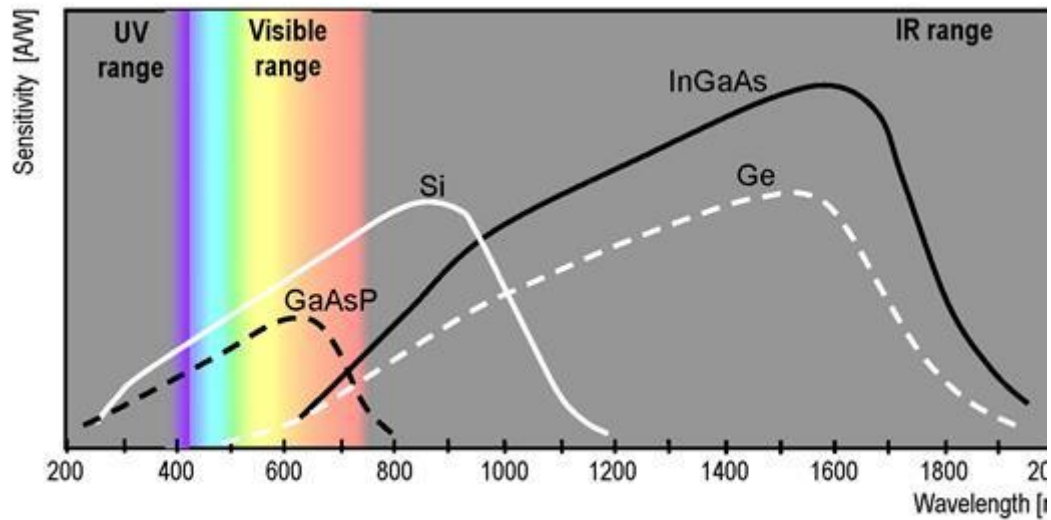
Figure 2.14. Frequency spectrum of different light sources



The spectrum of the tungsten filament lamp spans from the UV to IR frequencies. The deuterium lamp has a relatively flat frequency characteristic in the UV range. LEDs radiate in a quite narrow frequency range and laser diodes radiate on a single frequency. Laser light is nearly ideally monochromatic. The white light has a continuous spectrum over frequency. Using prism or optical grating white light can be refracted and the necessary wavelength can be selected with a displaceable slit (monochromator). The radiation spectrum can be modified in a simpler (cheaper) way by using optical filters. The selectivity of this procedure lags behind the monochromator.

2.2. Optical detectors

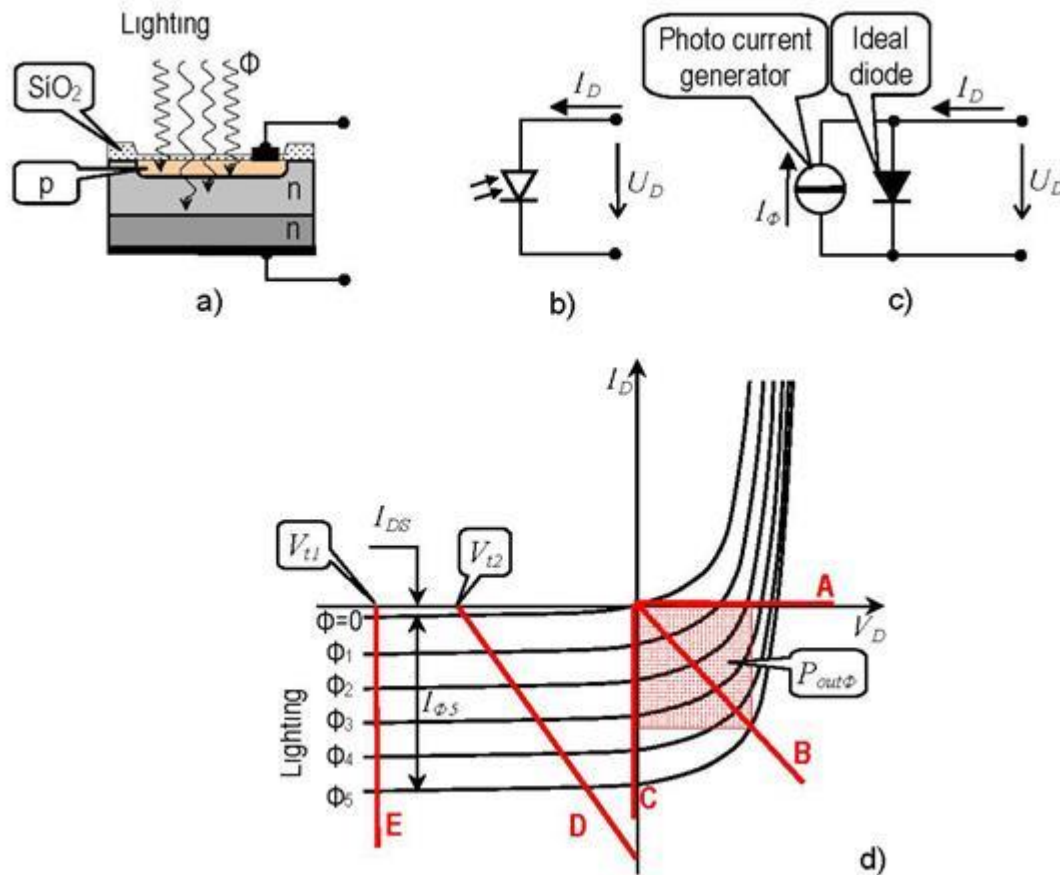
Figure 2.15. Sensitivity over wavelength for different semiconductors used for manufacturing optical detectors. Characteristics can be further influenced by the material of the window used during packaging.



Optical sensors make use of the photoelectric effect. Electrons in the sensor material absorb the energy of photons in the light beam. If the energy of an electron becomes high enough it ejects from the material. The energy of the photon depends on the wavelength; the energy necessary for ejection depends on the composition of the sensor material. Spectral sensitivity of optical sensors mainly depends on the selected material [2.14], [2.15], [2.16].

Photodiodes are planar diodes that are manufactured so that light beam can easily reach the p-n junction.

Figure 2.16. Cross section (a), symbol with voltage and current direction (b), model (c) and characteristics (d) of a photodiode. Load lines belonging to different modes of operation are also given.



Photons of the light beam Φ getting through the sensor window penetrate to the semiconductor near the p-n junction (see Figure 2.16.a). Their energy is conveyed to electrons that can be ejected resulting in an I_{Φ} current proportional to the incident radiation. This current is modelled by a current source (I_{Φ} , Figure 2.16.c). The operation of the photodiode is characterised by the current – voltage diagram given in Figure 2.16.d. In complete darkness ($\Phi=0$) we get the characteristics of the (rectifier) planar diode. In this application the $I_{DS}= 10$ pA – 1 nA (temperature dependent) reverse leakage current is called dark current.

Circuits for photodiodes

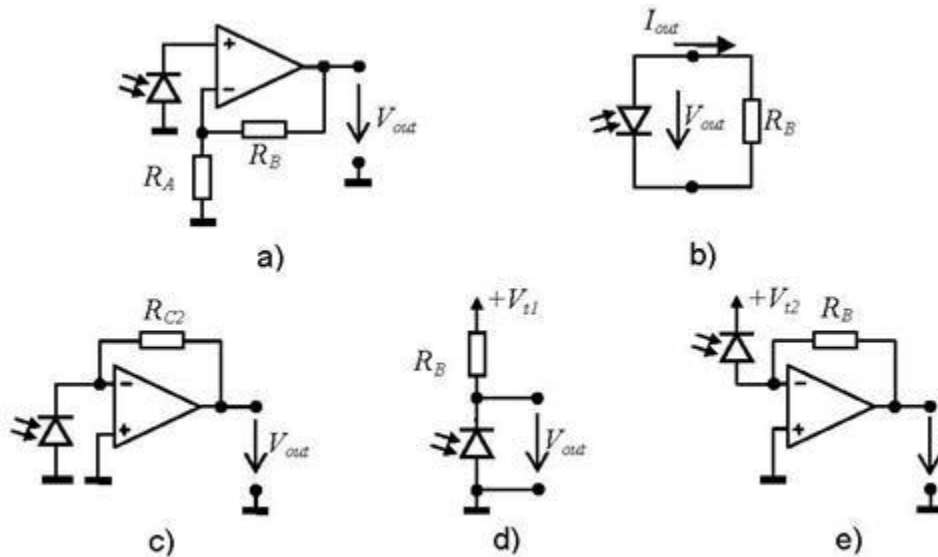
Figure 2.17 shows circuits realizing load lines in Figure 2.16.d. Circuit in Figure 2.17.a results in load line **A** that is a radiation meter with logarithmic characteristics. The circuit is able to operate while the energy of the incident radiation changes 5-6 orders of magnitude.

$$V_{out} = \frac{R_A + R_B}{R_A} V_D = \frac{R_A + R_B}{R_A} \frac{kT}{q} \ln \left(\frac{I_{\Phi}}{I_S} + 1 \right) \quad (2.19)$$

where k is Boltzmann constant, $q = 1.6 \times 10^{-19}$ C.

Load line **B** belongs to the photocell operation. The electrical energy produced is proportional to the area of the quadrangle shown ($P_{out\Phi}$). The produced electrical energy (area of the quadrangle) at a given radiation (Φ_5) will be maximal applying the optimal load line. Circuits shown in Figure 2.17. c, d, e result in load lines **C**, **D**, **E** respectively. These circuits generate output voltage proportional to the incident light.

Figure 2.17. Circuits realizing different modes of operation of the photodiode. Circuit with logarithmic characteristics (a). Photocell producing electrical energy (b). Circuits with linear characteristics (c, d, e).



Phototransistors

Phototransistors have higher sensitivity than photodiodes. Phototransistors are bipolar transistors; their BC p-n junction operates as a photodiode. Packaging and the surface of the chip are fabricated to ensure that incident light reaches the BC p-n junction. Photocurrent acts as base current. The collector current is much greater, $I_C = (B+1)I_0$, but the response time of the phototransistor is also much (B times) longer. The base of a phototransistor is usually open. Connecting a resistor between B and E the operation can be shifted from phototransistor (open circuit between B and E) to photodiode (short circuit between B and E). Because of the necessary U_{CE} voltage, phototransistors can be applied only in circuits shown in Figure 2.17. d and e.

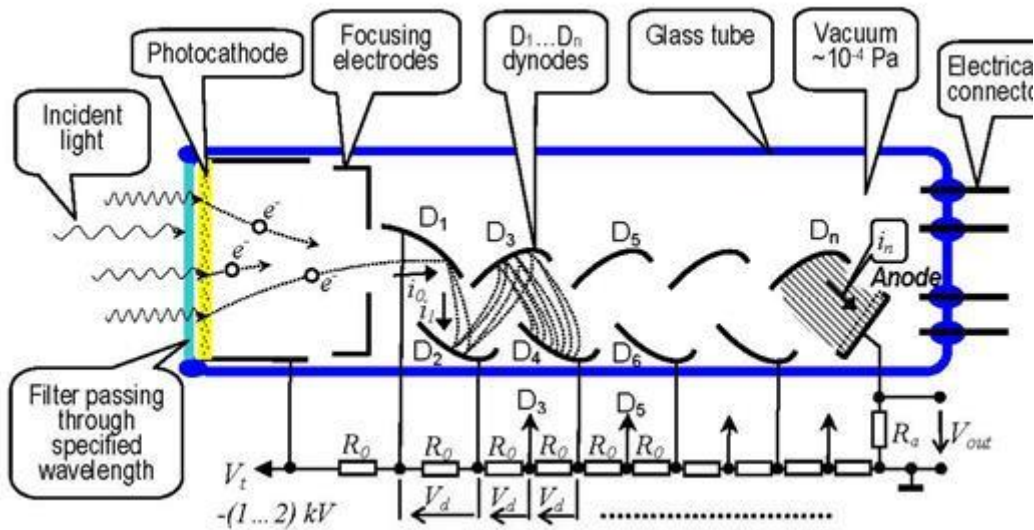
Photomultiplier tube

Photomultiplier tube comprises a vacuum tube, a photoemissive surface and an electron multiplier [2.17], [2.18]. Its schematic diagram is shown in Figure 2.18. Electrons are moving freely in the 10^{-6} mmHg vacuum towards the positive electrode. Incident radiation reaches the photocathode through a window of the tube. The sensitivity over wavelength is determined by the characteristics of the window and wavelength dependence of the emission at the photocathode. Each photon with a sufficient energy frees (dislodges) an electron. Emitted electrons focused into a narrow beam fly towards the more positive D_1 dynode. Dynodes are covered with material of good secondary emission thus each electron reaching a dynode causes the emission of several (5 – 10) electrons, depending on the voltage difference between neighbouring dynodes ($V_d = 100...150$ V). The current is multiplied at each dynode. The output current i_n is given by eq. 2.20.

$$i_n = i_0 g^n \quad (2.20)$$

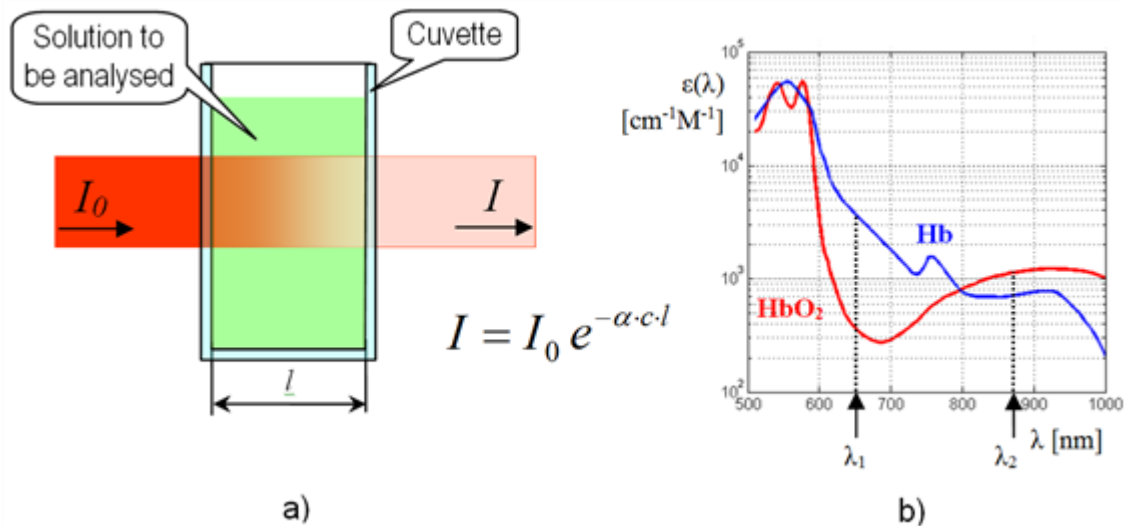
The multiplication factor g is 5 – 10, n is the number of dynodes, 9 – 12. The resulting current amplification is in the order of 10^6 . Electrons are distracted by the magnetic field of the Earth, so photomultiplier tubes are magnetically shielded. These tubes have high sensitivity, small noise and low response time. They are rarely used as they are much more expensive and require a more sophisticated application than semiconductor sensors.

Figure 2.18. Schematic and theory of operation of a photomultiplier tube. Between dynodes $D_1 \dots D_4$ the electron multiplication is drawn for $g = 2$.



2.3. Light absorption

Figure 2.19. Light absorption in solutions (a). The extinction coefficient of haemoglobin and oxyhaemoglobin as a function of wavelength (b).



Absorption of light is used to measure concentration of solutions by measuring the ratio of outgoing and incoming light intensity [19]. Neglecting scattering, luminescence and too high concentration the ratio is given by Beer-Lambert law:

$$I = I_0 e^{-\alpha c l} \quad (2.21)$$

where:

α = absorption coefficient [$\text{cm}^{-1} \text{M}^{-1}$]

c = concentration [mol/litre = M]

d = distance travelled by light in the solution [cm].

Only the absorption coefficient depends on wavelength, the effect of concentration c and distance d are independent of each other and of the wavelength. Equation 2.21 can be written using power of 10:

$$I = I_0 10^{-\varepsilon cl} \quad (2.22)$$

where ε = molar absorption coefficient [$\text{cm}^{-1} \text{M}^{-1}$], $\varepsilon = 0.434\alpha$

Transmittance T [%] is the ratio of the outgoing and incoming intensity, see eq. 2.23.

$$T = \frac{I}{I_0} = 10^{-\varepsilon(\lambda)cl} \quad (2.23)$$

The absorbance A (dimensionless) is the logarithm of transmittance, see eq. 2.24.

$$A = \lg\left(\frac{I_0}{I}\right) = \varepsilon(\lambda)cl \quad (2.24)$$

The solution to be measured is in a transparent cuvette. Its material (glass, plastic or quartz) has small absorption at the used wavelengths.

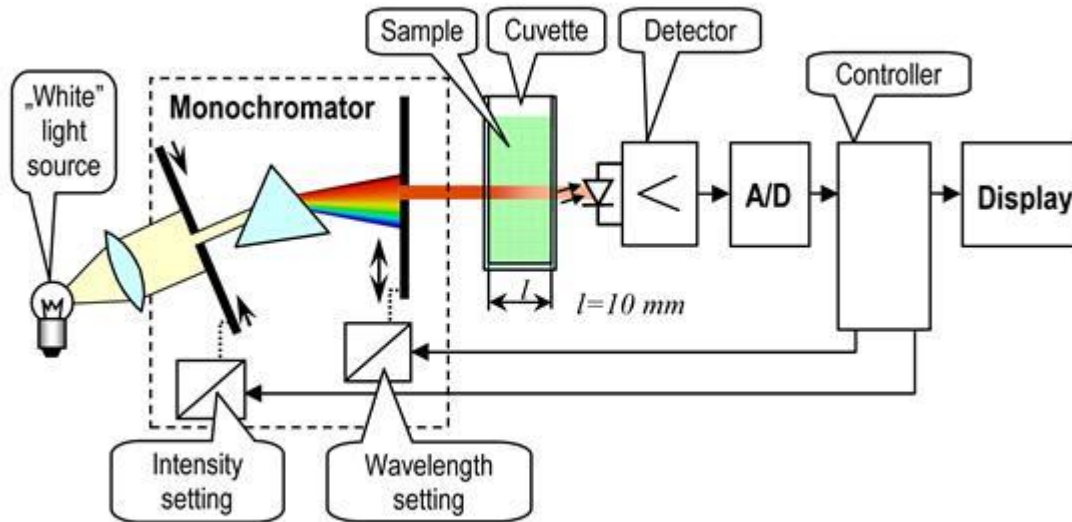
Most common applications:

1. Measurement of concentration, when the components are known. Measurement is performed at given wavelength(s), on which the tested component has characteristic and strong absorption. Such a device is called photometer.
2. Identification of the components in the solution. Complete absorption spectrogram is measured, characteristic absorption patterns are searched for. Such a device is called spectrophotometer.

2.4. Spectroscopes

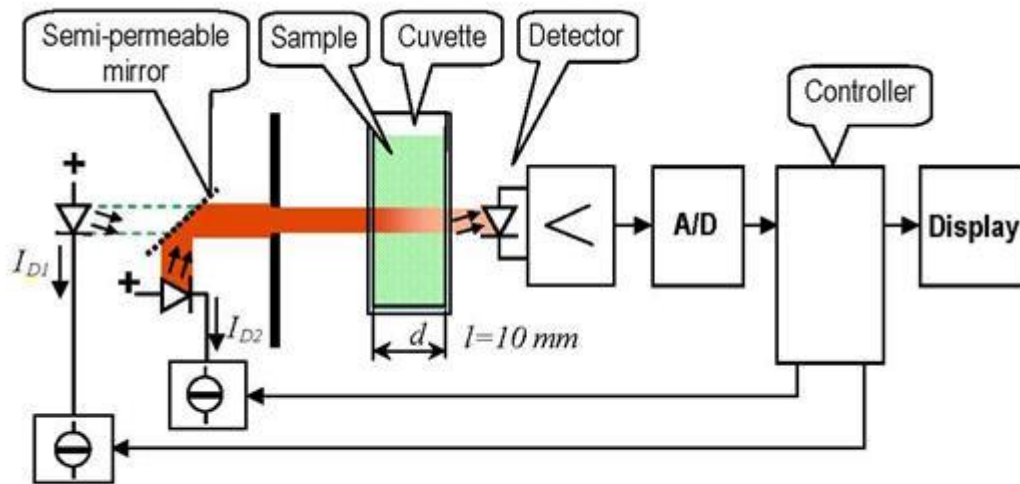
Spectrophotometer Its schematic is given in Figure 2.20. Within its range it uses continuously changing wavelength. The monochromator selects a narrow band of wavelength from a wider range. The light (radiation) of selected band passes through the cuvette and the solution in it and reaches the detector that gives an output signal proportional to the detected intensity. The analogue output signal is converted to digital data and then the absorption is calculated. This requires the knowledge of the I_0 intensity of the signal reaching the cuvette. Changing the wavelength in small steps the device produces the absorption spectrum (see Figure 2.19. b). The double beam spectrophotometer splits the output light of the monochromator into two beams, one passing through the cuvette with the solution to be tested and the other one – the reference signal – passing through an empty cuvette. The intensity of both beams is measured. Calculating the ratio of the two intensities eliminates the I_0 intensity. Both single- and double beam spectrophotometers offer relative measurement, when the absorbance of a known solution is set as reference and absorbance of the unknown solution is expressed as percentage of the known solution.

Figure 2.20. Schematic of the spectrophotometer. The monochromator selects a narrow wavelength light from „white light”.



Colorimeters, photometers are simpler devices than spectrophotometers. Only a few discrete wavelengths are available, generated by LEDs or colour filters (see Figure 2.21). The aim is to detect the presence or measure the concentration of a certain component. Handheld colorimeters are available.

Figure 2.21. Schematic of a colorimeter that uses two wavelengths, generated by two separate LEDs.



2.5. Pulse oximeter

Measurement of the oxygen saturation of arterial blood is often necessary. Pulse oximeter measures oxygen saturation (normal range: 94 – 99%) non-invasively. Oxygen saturation (SpO_2) is the ratio of oxyhemoglobin to the total concentration of hemoglobin present in the blood, see eq. 2.25.

$$\text{SpO}_2 [\%] = \frac{\text{HbO}_2}{\text{HbO}_2 + \text{Hb}} 100\% \quad (2.25)$$

where:

HbO_2 amount of haemoglobin combined with oxygen (oxyhaemoglobin)

Hb amount of haemoglobine without oxygen.

Oxygen saturation expresses the percentage of haemoglobin carrying oxygen to all haemoglobin (see eq. 2.26).

$$SpO_2[\%] = \frac{c_{HbO_2}}{c_{HbO_2} + c_{Hb}} 100\% \quad (2.26)$$

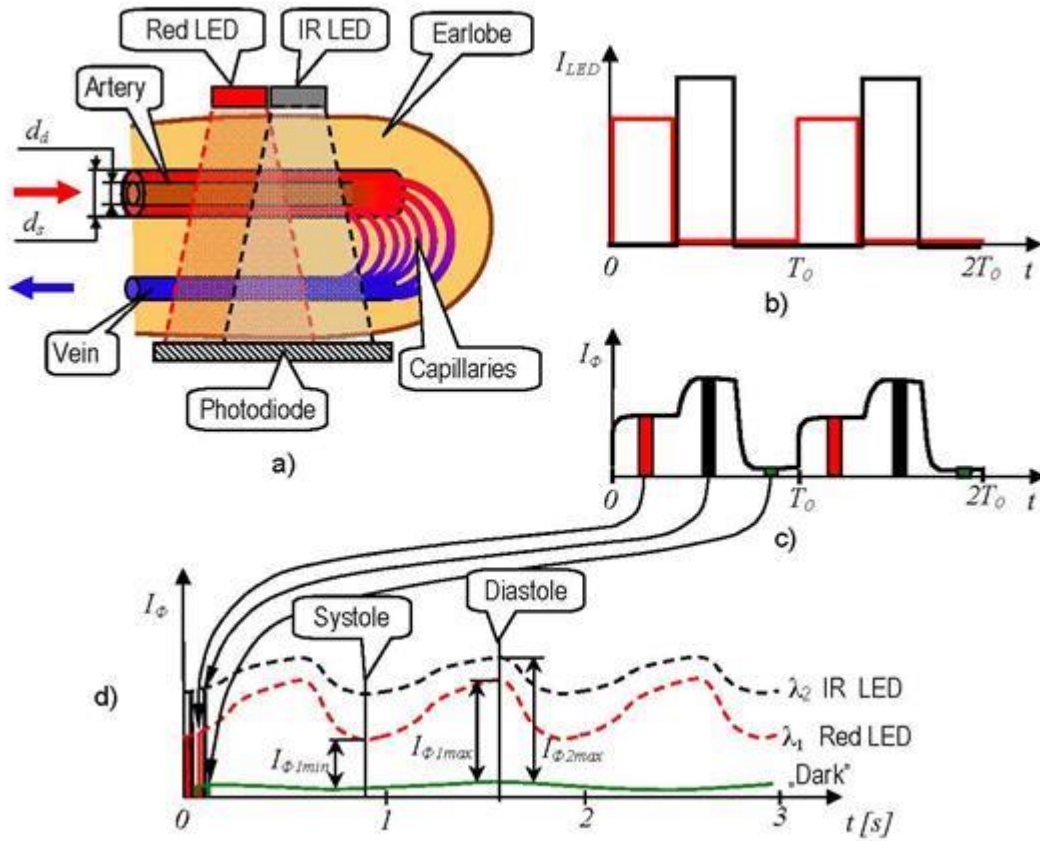
Figure 2.19.b clearly shows that absorption of Hb and HbO_2 is significantly different at wavelengths indicated by arrows (λ_1 and λ_2). The measurement set-up given on Figure 2.22a makes use of this [2.20]. It is enough to place the sensor on the fingertip or earlobe of the tested person. The sensor contains a photodiode and two LEDs that emit light through about the same part of the tested body segment. The body segment contains skin, tissues but also arteries, veins and capillaries. The conditions necessary for photometry are not met: the tested material is not homogenous, contains unknown components, the thickness of layers is also unknown and scattering cannot be neglected. The idea is to make use of the pulsation of the artery.

The three phases of the operation of LEDs are illustrated in Figure 2.22.b: no LED on (dark phase), IR LED on, red LED on. During the dark phase environmental light is measured for later compensation by subtraction. Cycle time T_0 is in the range 1 – 10 ms. The light intensity vs. time at the photodiode is shown in Figure 2.22.c. From the sampled – and amplified – signal the time function of the sensed infrared and red light can be restored, see Figure 2.22.d. The diameter of the artery changes during every heart cycle thus changing the absorption of arterial blood. Sampling frequency is much higher (~ 1 kHz) than frequency of a beating heart (~ 1 Hz). The light intensity sensed by the photodiode is estimated as

$$I_{\phi D} = I_{\phi LED} e^{-\sum \varepsilon_i(\lambda) c_i l_i} \quad (2.27)$$

where c_i is the concentration, l_i is the thickness and $\varepsilon_i(\lambda)$ is the absorption on wavelength λ of the i^{th} component.

Figure 2.22. The scheme of pulse oximetry. IR and red light beams across the earlobe, artery diameter during systole and diastole (a). Time function of LEDs light intensity (b) and intensity sensed by the photodiode (c). The intensity vs. time functions of the LEDs restored from the samples during three heart cycles (d).



The pulsation of the artery changes its diameter while the diameter of veins remains constant. The constant part of absorption is caused by tissues and veins (if fingertip is transilluminated then also by the nail) and by the artery when its diameter is minimal. The change in absorption is caused by the change of the diameter of the artery. When the red LED is on, $\lambda_1=650$ nm wavelength incident light beam is detected by the photodiode: $I_{\phi 1min}$ is the minimal and $I_{\phi 1max}$ is the maximal intensity. The difference of the two intensities is caused by the change in the diameter of the artery: $\Delta d = d_s - d_d$. The ratio of the two intensities (see eq. 2.28) eliminates the absorption by tissues with unknown thickness and concentration, but also the intensity of the emitted light and the optical-to-electrical conversion factor of the photodiode.

$$\frac{I_{\phi 1min}}{I_{\phi 1max}} = e^{K_1} \quad (2.28)$$

The exponent in detail:

$$K_1 = -\Delta d \left(\epsilon_{Hb1} c_{Hb} + \epsilon_{HbO_2 1} c_{HbO_2} \right) \quad (2.29)$$

The same ratio is calculated when the IR LED ($\lambda_2=870$ nm) is on:

$$\frac{I_{\phi 2min}}{I_{\phi 2max}} = e^{K_2} \quad (2.30)$$

$$K_2 = -\Delta d \left(\epsilon_{Hb2} c_{Hb} + \epsilon_{HbO_2 2} c_{HbO_2} \right) \quad (2.31)$$

Taking the K_1/K_2 ratio the unknown Δd is also eliminated. The resulting fraction contains only two variables with unknown values: c_{Hb} and c_{HbO_2} . Although their values cannot be calculated, their ratio is enough for SpO_2 .

$$\text{SpO}_2[\%] = \frac{1}{1 + \frac{c_{\text{Hb}}}{c_{\text{HbO}_2}}} 100\% \quad (2.32)$$

The simplified derivation proves that the method is able to determine SpO_2 . Pulse oximeters are able to measure oxygen saturation with a few percent accuracy. Usually the important diagnostic information is the change in oxygen saturation which can be detected with higher accuracy.

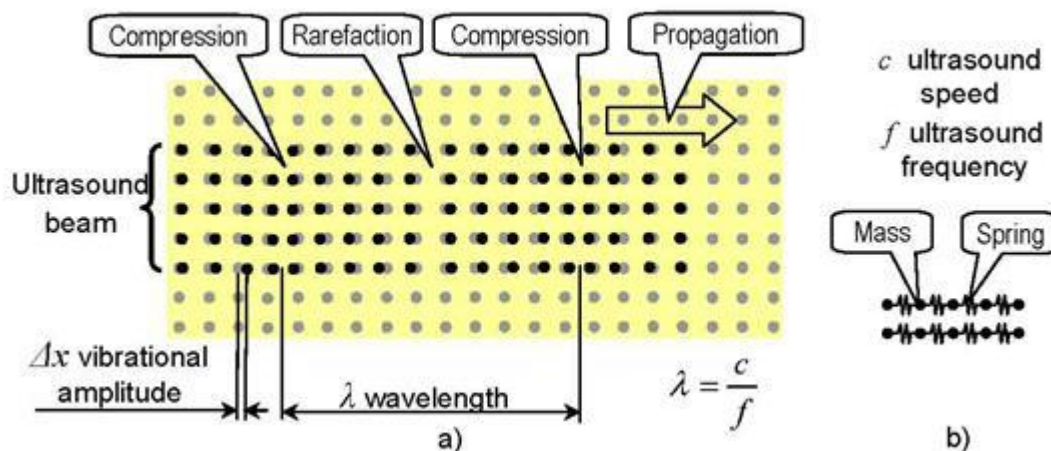
3. Diagnostic application of ultrasound

3.1. Properties of ultrasound

Ultrasound is a mechanical vibration – cyclic sound pressure wave – with a frequency above human hearing range [2.21], [2.22], [2.23/], [2.24]. Ultrasound is non-ionizing radiation. As low intensity is enough in biomedical applications, there are no known adverse heating or pressure effects in tissues. However, the American Pregnancy Association states: „*The long term effects of repeated ultrasound exposures on the foetus are not fully known. It is recommended that ultrasound only be used if medically indicated.*” The main risk is the cavitation effect of ultrasound that is made use of during pipe cleaning.

Figure 2.23 illustrates how ultrasound propagates in homogenous material or in tissue. Let's suppose the material at rest is divided into uniform volume elements denoted with light grey dots. The volume elements shift from their resting position along the direction of the traversing ultrasound, i.e. it is a longitudinal wave. Volume elements vibrate around their resting position while ultrasound passes by.

Figure 2.23. Vibration of volume elements as ultrasound wave traverses (a) and mechanical model of the phenomenon (b)



For the sake of illustration, the amplitude of vibration, Δx is exaggerated in Figure 2.23 compared to the wavelength. For diagnostic purposes 2 – 20 MHz frequency (wavelength 0.75 – 0.075 mm in tissues) ultrasound is used. Objects smaller than the wavelength of ultrasound cannot be detected. This would explain selecting high frequency for the test. However, attenuation increases with the square of frequency! Selection of the frequency means optimization between spatial resolution and imaging depth. The mechanical power through unit area is called intensity (I). The usual intensity in bio imaging is $I = 0.1 \dots 100 \text{ mW/cm}^2$. The maximum local shift of volume elements is $\Delta x = 5\text{-}50 \text{ nm}$.

The supposed volume elements can be modelled by a concentrated mass and elastic connections between neighbours (see Figure 2.23.b). The measure of elastic connection is compressibility (κ), the mass of a supposed volume element is determined by the density (ρ) of the material. The propagation velocity of ultrasound (c) depends on these parameters, see eq. 2.33.

$$c = \frac{1}{\sqrt{\rho \kappa}} [\text{m/s}] \quad (2.33)$$

where:

κ compressibility [m^2/N]

ρ density [kg/m^3]

Acoustic impedance is another important parameter of the material in which ultrasound propagates. This is the ratio of local dynamic forces and displacements; it characterizes the ability to convey vibration. The value is defined as the ratio of density and compressibility, see eq. 2.34.

$$Z_A = \sqrt{\frac{\rho}{\kappa}} [\text{Rayl}] \quad (2.34)$$

Velocity and density can be measured easily (contrary to compressibility). Transforming eq. 2.34 we get a formula for acoustic impedance that fits better to practical calculations, see eq. 2.35.

$$Z_A = \sqrt{\frac{\rho}{\kappa}} = \sqrt{\frac{\rho^2}{\rho \kappa}} = \rho \frac{1}{\sqrt{\rho \kappa}} = \rho c \quad (2.35)$$

The unit of acoustic impedance is: $\frac{\text{kg}}{\text{m}^3} \frac{\text{m}}{\text{s}} = \frac{\text{Ns}}{\text{m}^2} = \text{Rayl}$.

Table 2.2. Acoustic properties of different materials

Material	c [m/s]	Z_A [$\text{kg}/\text{m}^2\text{s} \times 10^{-6}$]	b [dB/(cmMHz)]
Air (20°C)	343	412×10^6	1,2
Water (20°C)	1480	1,48	0,0022
Oil (SAE 20/30)	1740	1,4	0,95
Blood	1570	1,6–1,7	0,18
Fat	1475	1,33	0,6
Soft tissue	1540	1,35–1,7	0,3–1,5
Brain	1560		0,85
Liver	1549–1570	1,65	0,9
Muscle	1580	1,7	1,2–3,3
Bone	3600	6,12	20
PZT piezoceramics	4000	31	
Brass	4440	36	
Aluminium	6320	17,1	8,4

3.2. Propagation of ultrasound

The intensity of ultrasound decreases as it propagates in homogenous material. The main reasons for the decrease are the following.

Absorption Particles of the material in which the ultrasound propagates vibrate and transfer vibration to neighbouring particles. Vibration converts part of the energy into heat. As a result the intensity of ultrasound beam decreases exponentially with distance, see eq. 2.36.

$$I_x = I_0 e^{-\beta x} \quad (2.36)$$

where:

I_0 intensity in initial position [W/m²]

I_x intensity after distance x [W/m²]

x distance from initial position [m]

β absorption factor [m⁻¹]

The ratio of the initial and actual intensity is denoted by Γ_x . This is expressed in dB (see appendix in chapter 3), thus the resultant attenuation of consecutive layers can simply algebraically summed, see eq. 2.37.

$$\Gamma_x[\text{dB}] = 10 \lg \frac{I_x}{I_0} = -bx \quad (2.37)$$

Attenuation expressed in dB is proportional to distance covered and attenuation factor b . b is a function of β absorption factor, see eq. 2.38.

$$b = 4.34\beta \text{ [dB/m]} \quad (2.38)$$

Ultrasound sensors give output signal proportional to sound pressure p . The relation between intensity and sound pressure is given by eq. 2.39.

$$I = \frac{p_{\text{eff}}^2}{Z_a} \left[\left(\frac{N}{m^2} \right)^2 \frac{m^3}{N_s} = \frac{W}{m^2} \right] \quad (2.39)$$

Expressing intensity attenuation with the ratio of amplitudes:

$$\Gamma_x[\text{dB}] = 10 \lg \frac{I_x}{I_0} = 10 \lg \frac{p_x^2}{p_0^2} = 20 \lg \frac{p_x}{p_0} \quad (2.40)$$

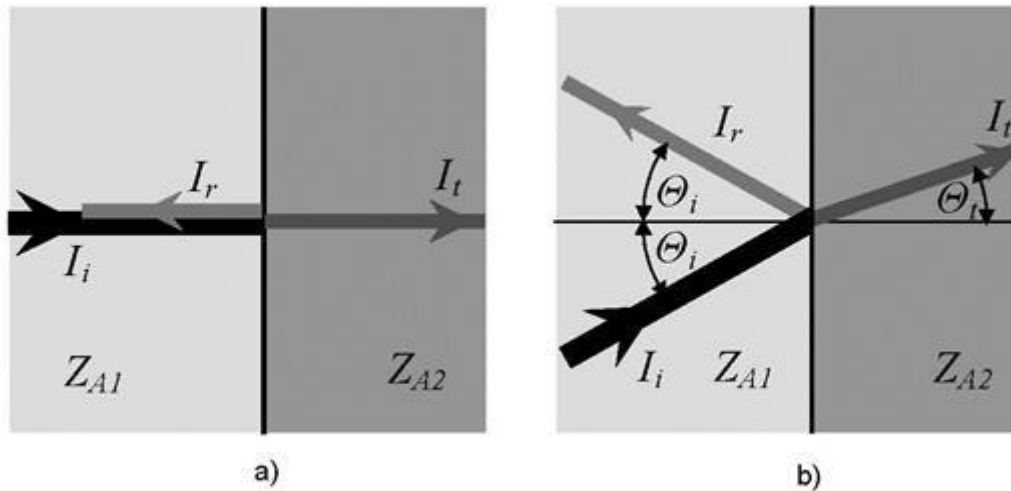
b attenuation factor in Table 2.2 refers to intensity. Absorption is frequency dependent, in solid material and in tissue absorption increases with frequency. According to Table 2.1 in liver $b=0.9$ dB/(cm MHz). For a 5 MHz ultrasound $b = 0.9 \times 5 = 4.5$ dB/cm. 10 cm propagation in liver means 45 dB attenuation! For a 1 MHz ultrasound propagation over the same distance means only 9 dB attenuation.

Scattering Changes – in size smaller than the wavelength of ultrasound – in the density, compressibility or absorption cause radiation of a scattered wave in all directions. This effect decreases the energy of the propagating beam and deteriorates contrast if ultrasound is used for imaging.

Divergence and convergence For diagnosis a focused beam is needed. The intensity of a focused beam decreases as a result of absorption and scattering. Spreading of the beam is called divergence. Spreading also decreases the intensity over unit area. Converging increases the intensity over unit area.

Reflection When ultrasound reaches the boundary of two materials with different acoustic impedance partial reflection happens. If the incident beam is perpendicular to the boundary then both the reflected and the transmitted beam remain in line with the incident beam (see Figure 2.24.a). The ratio of intensities (reflected beam over incident beam) is the reflection coefficient, R .

Figure 2.24. Reflection and transmission of ultrasound at the boundary of two materials with different acoustic impedance. Perpendicular (a) and angular (b) incident light.



$$\frac{I_r}{I_i} = R = \left(\frac{Z_{A2} - Z_{A1}}{Z_{A2} + Z_{A1}} \right)^2 \quad (2.41)$$

The ratio of transmitted and incident light intensity is given by eq. 2.42.

$$\frac{I_t}{I_i} = \frac{4Z_{A2}Z_{A1}}{(Z_{A2} + Z_{A1})^2} \quad (2.42)$$

At fat-muscle boundary: $I_r = 0.015I_i$, $I_t = 0.985I_i$.

At angular incident light the beam is refracted and the measure of reflection depends on the angle (see Figure 2.23.b).

$$R = \frac{I_r}{I_i} = \left(\frac{Z_{A2} \cos \theta_i - Z_{A1} \cos \theta_t}{Z_{A2} \cos \theta_i + Z_{A1} \cos \theta_t} \right)^2 \quad \text{and} \quad \frac{\sin \theta_i}{\sin \theta_t} = \frac{c_1}{c_2} \quad (2.43)$$

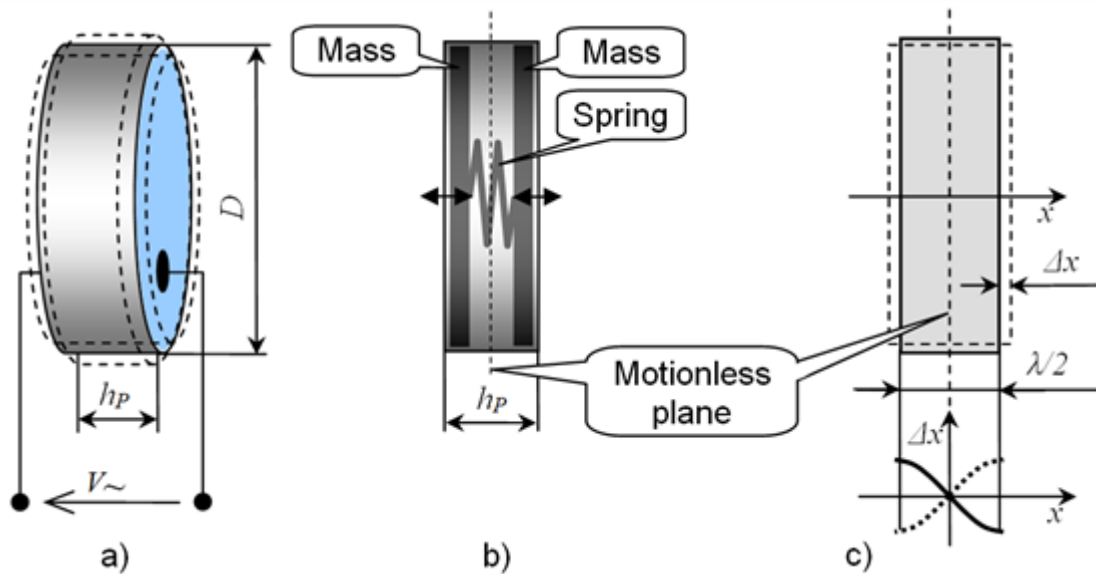
(Reflection coefficients 2.41 – 2.43 refer to intensity. By taking the square root we can get the reflection coefficient for pressure amplitudes, see eq. 2.40.) Diagnostic ultrasound detects and visualizes the boundaries of organs and tissues with different acoustic impedance using the impulse echo method. Most often the transmitter and receiver is the same element. The emitted ultrasound beam is reflected from boundaries as described above. The reflected signal – echo – arrives at the transducer after a delay depending on the distance between the transducer and the reflecting boundary. The amplitude of the echo is high if the beam is perpendicular to the boundary and the difference in acoustic impedances of the two materials is substantial. In this latter case this also means that most of the incident beam is reflected, layers behind the boundary can hardly be detected.

From boundaries where there is air on one side the reflection is nearly 100% because the acoustic impedance of air is about 10^8 times greater than the acoustic impedance of water or body fluids. Air is not allowed between the sensor head and the tested anatomic layers. In medical practice gel is used to fill out the gap between skin and sensor head.

3.3. Generating and sensing ultrasound

In the transducer head most often PZT ceramics is used (see 2.1.4) to generate and sense ultrasound [2.25], [2.26]. Figure 2.25.a illustrates the change in thickness of a piezoceramic disk as voltage is applied across its flaps. The change is very small, in the order of 10 ... 100 nm. (Volume remains constant, thus the diameter also changes.) The voltage to mechanical change and vice versa is effective if its frequency is equal to the own mechanical resonance frequency of the disk. A freely standing three dimensional solid body has several resonance frequencies. The favourable resonance results in effective beam transmission in line with the axis of the disk.

Figure 2.25. Deformation (exaggerated) of a piezoceramic disk during ac excitation (a), the simplest model of the vibrating system (b) and the deformation along the x axis (c).



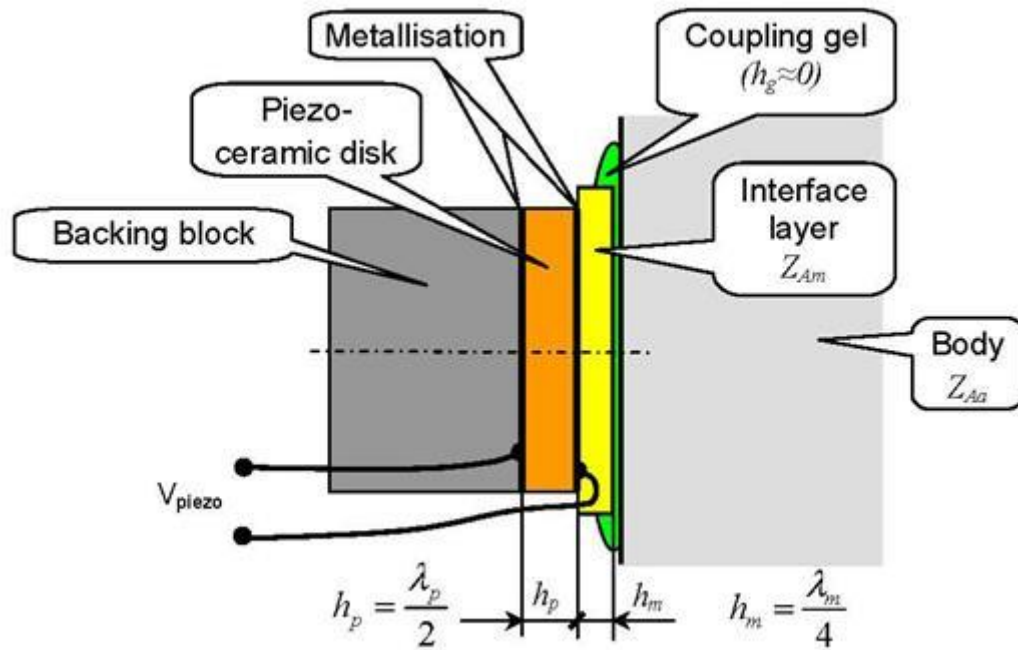
The simple model in Figure 2.25.b. comprises two masses and a connecting spring. The two masses move in opposite direction. The vibration amplitude is maximal when the frequency of the excitation signal equals the resonance frequency (f_0) of the disk. f_0 depends on the h_p thickness. Mass increases while the stiffness decreases with thickness. In a real disk the mass and the spring is dispersed and only the midplane stands still. Vibration amplitude of inner layers are shown in Figure 2.25.c. Applying its resonance frequency (f_0) to a h_p thick disk the vibration pattern will be half wavelength standing wave. Δx displacement (and vibration amplitude) is zero in the midplane and maximal at the cover planes. The wave reflects from the cover plane in-phase. In Figure 2.25.b the concentrated, in 2.25.c the dispersed model is given of the same resonance. The vibration of one of the cover planes must be transferred to the material to be tested. The opposite cover plane must be fixed with attenuating layer to inhibit radiation towards that direction and to aid fast settling down following excitation.

The acoustic impedance of PZT ceramics and body tissues greatly differ. As a result, about eighty percent of the ultrasound reflects from the boundary. The same is true for the reflected ultrasound. As a result, without acoustic coupling between the transducer and the human body only maximum 4% of the generated signal would get back to the transducer. Figure 2.2.6 shows how to apply an acoustic coupling layer with thickness $\lambda/4$. This layer is embedded in the transducer head. Acoustic coupling is optimal if the acoustic impedance of the coupling layer Z_{Am} equals the geometric mean of the acoustic impedances of the two layers to be coupled, see eq. 2.44.

$$Z_{Am} = \sqrt{Z_{Ap}Z_{At}} \quad (2.44)$$

In ideal case coupling does not cause intensity loss. In real applications some intensity loss is unavoidable but the improvement compared to not using coupling can be as high as 5 ... 10-fold.

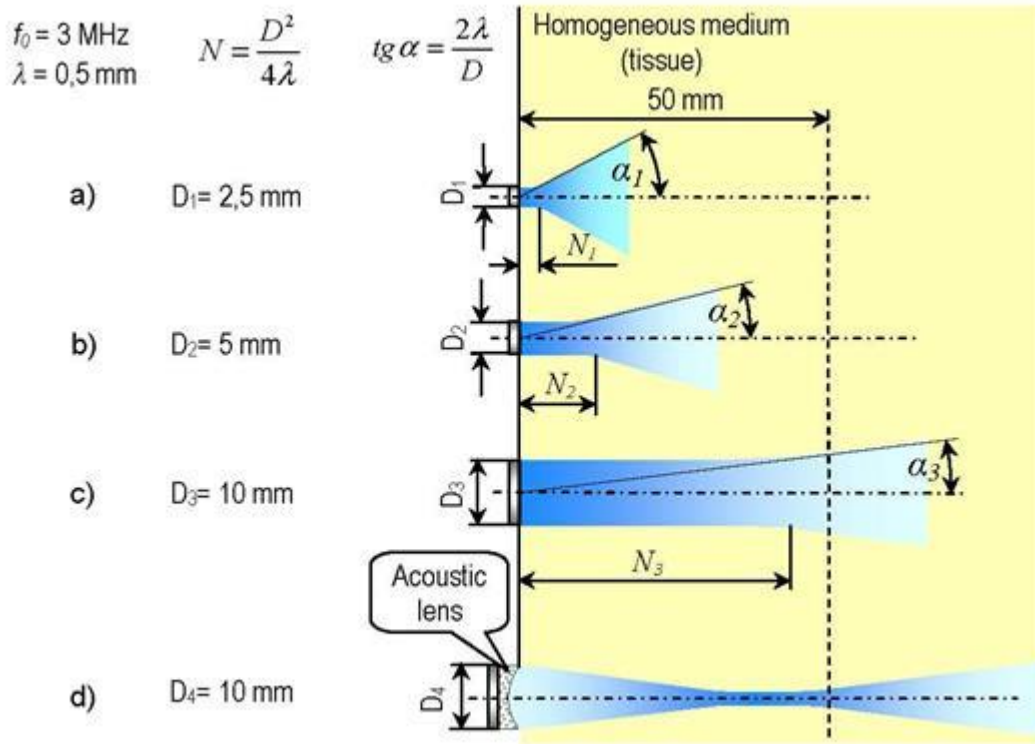
Figure 2.26. Schematic of an ultrasound transducer and its coupling to the human body



3.4. Beam profile

The vibration of the cover layer of the piezoceramic disk generates an ultrasound beam with the same diameter. Until distance N (called near-field or Fresnel zone) the beam is parallel further in the far-field (Fraunhofer zone) it diverges with half-cone angle α . Figure 2.27 shows the shape of beams transmitted from disks with different diameter. In practice intensity along the cross section of the beam is inhomogeneous: maximal in the midline; decreases outwards. Good resolution requires small diameter beam in the depth of the object to be tested. Figure 2.27 a. – c. shows that simply reducing the diameter of the disk does not result in a few mm beam diameter 5 to 10 cm far from the transducer. It is also important to be noted that the same profile applies for the echo! The beam can be acoustically focused to small diameter cross section at a distance from the transducer. Figure 2.27.d illustrates that different transducer heads are needed to detect objects at different distances from the body surface when acoustic focusing is applied. Electrical (dynamical) focusing makes it possible to use the same sensor for different distances.

Figure 2.27. Beam profile (a, b, c) of piezoceramic disks with different diameter (same wavelength) and focusing with acoustic lens (d)

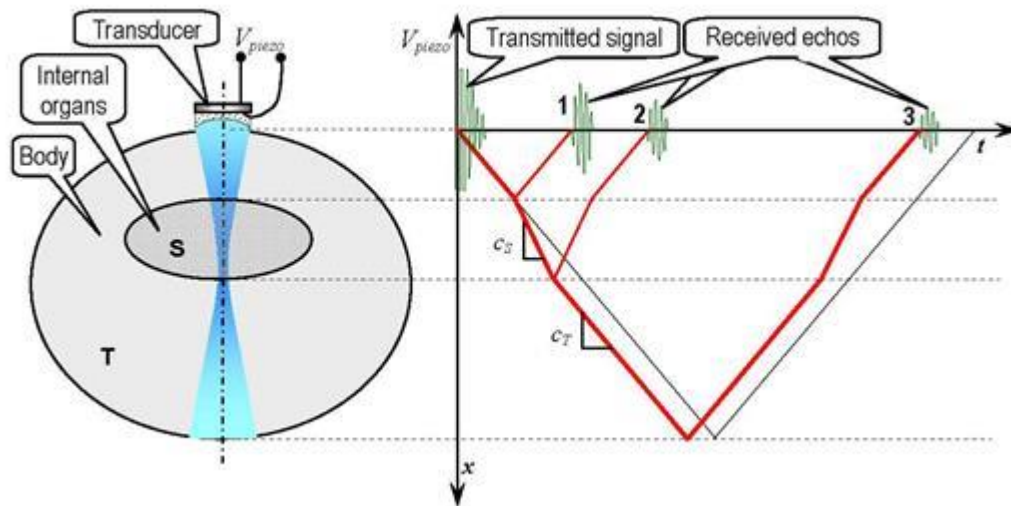


3.5. Pulse – echo response

The piezoelectric disk or plate is excited by the transmitter [2.28], [2.29], [2.30]. Most commonly used excitation is ultrasound pulse comprising 3...6 periods of ultrasound frequency sine wave with a few hundred volts amplitude. Figure 2.28 shows that the V_{piezo} excitation signal is converted to mechanical vibration transmitting ultrasound wave. The wave propagates with c_T velocity in the body **T** to be tested. The wave is reflected from the boundary of the organ **S** because of the different acoustic impedance ($Z_{AT} \neq Z_{AS}$). The displacement-time function to the right of Figure 2.28 illustrates the propagation of the pulse. The reflected signal (echo) is sensed by the same transducer that transmitted the pulse. Echo signals 1, 2, 3 are converted into electrical signal (voltage). The voltage generated by the echo must be amplified (and filtered), its amplitude is much smaller than the amplitude of the excitation signal. The echo signal can be visualized by an oscilloscope. Either a storage oscilloscope is needed or the excitation must be repeated periodically. The next excitation must not be started before the arrival of the echo from the farthest reflection. The horizontal axis of the echo time also refers to the distance from the transducer (depth in the body). This kind of visualization of the echo signal is called **A-mode** (Amplitude mode). In Figure 2.28 the propagation velocity in organ **S** is greater than in the surrounding tissue ($c_s > c_T$). This distorts the distance of the layers behind organ **S**.

The thinner is organ **S** the closer are echo signal 1 and 2. The depth (radial) resolution is reached when echo signals 1 and 2 start to overlap. Overlap prevents the measurement of thickness of a layer. Similarly, the end of transmission and the first echo signal must not overlap. This determines a minimal distance from the body surface that can be examined with the pulse-echo method. Layers closer than that are in the dead space. An animation is available about the pulse-echo method at the following address: http://project.mit.bme.hu/kobak2012/ultrasound_pulse_echo.pps

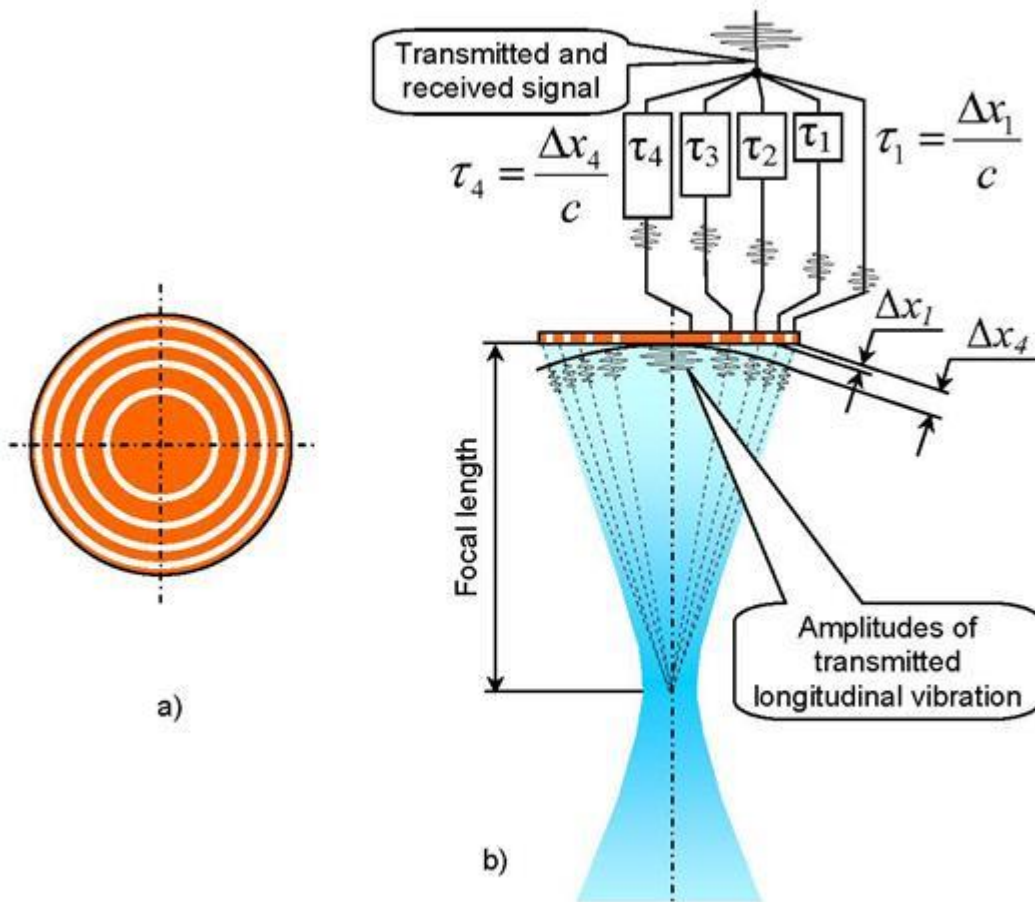
Figure 2.28. Signal generated by the pulse-echo method



In order to increase resolution the ultrasound pulse can be shortened using less cycle. This reduces the energy of the pulse and thus deteriorates the detectability of the echo. Increasing the frequency of the ultrasound also shortens the ultrasound pulse but at the same time increases the absorption in the tissue which decreases the penetration depth.

Dynamic focusing is done by dividing the disk into concentric rings and applying the excitation signal to the rings with delay, see Figure 2.29. The outer ring gets the excitation signal first; further rings get with ever longer delay. The waves transmitted by the different rings interfere so that towards the focus strengthening, in any other direction weakening happens. Changing the delay times changes the distance between the transmitter and the focus. The beam profile remains unchanged during echo if delay times remain unchanged.

Figure 2.29. Electronic (dynamic) focusing of ultrasound beam. The cross section of the piezoelectric disk divided into rings (a), and the beam after focusing by delayed control signal (b).

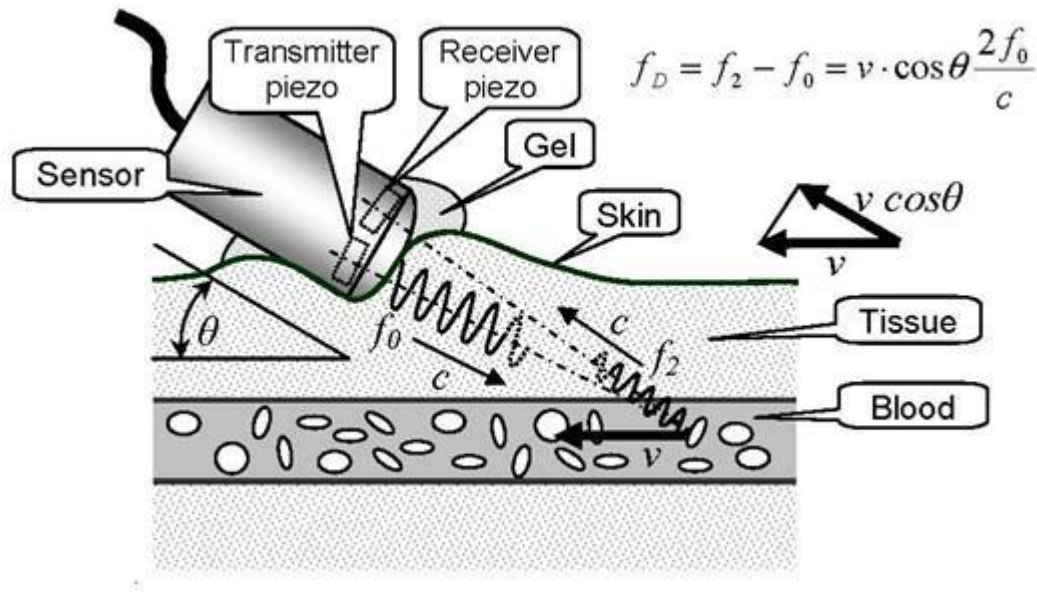


3.6. Applying the Doppler-effect

The frequency of the echo signal reflected from a moving object deviates from the frequency of the transmitted signal (f_0). Flow measurement can be based upon this phenomenon [2.31], [2.32]. The simple blood flow meter has a separate transmitter and receiver. The frequency of the transmitted signal is constant (f_0), the frequency of the received signal is f_2 (see Figure 2.30). If f_0 is between 4 ... 8 MHz then the $f_2 - f_0$ frequency difference caused by moving formed particles in blood will be in the audible range. The operator can draw conclusions from the sound to flow. This is called D-mode (Doppler audio mode).

The transmitted beam is at an angle with the direction of the flow so the projection of flow (velocity) will be measured. (Flow perpendicular to beam direction cannot be measured.) More complex devices calculate flow velocity and display also its direction (approaching or driving away). Doppler-effect is made use of in the echo mode of sophisticated ultrasound imaging devices, denoting different velocities by colouring.

Figure 2.30. Measuring blood flow based on Doppler effect



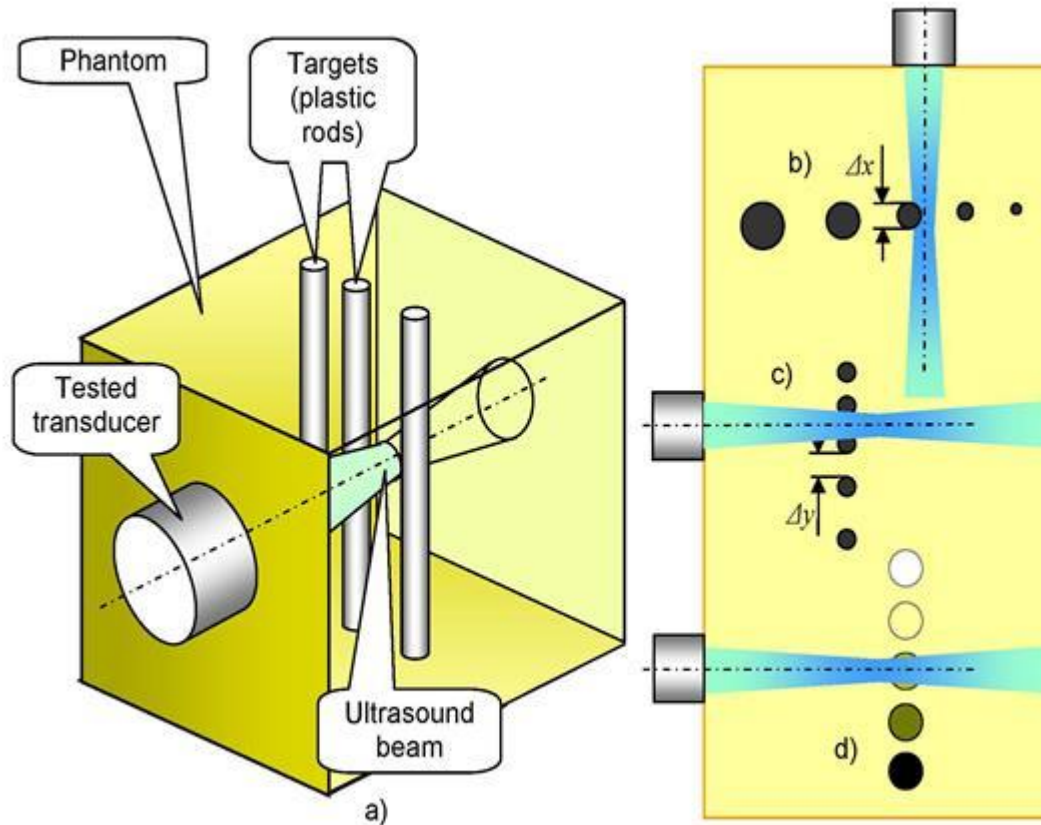
3.7. Qualifying the pulse echo method

Diagnostic ultrasound devices are tested using phantoms [2.33]. Standardized qualifying procedure independent of manufacturers has not been agreed upon. Phantoms are rectangular prisms with acoustic impedance similar to tissue (e.g. rubber container filled with water) with different objects (plastic rods and strings) in a known position, see Figure 2.31.a. By processing the echo from the objects the following parameters can be tested: direction of the beam, accuracy of distance measurement, distance to the focus, and depth of dead space.

An important feature is the smallest detectable tissue element with acoustic impedance different from the surroundings. The smallest detectable layer thickness or diameter in line with propagation can be characterized by Δx radial (also called axial or range) resolution (see Figure 2.31.b). Lateral resolution is characterized by the smallest distance (Δy , lateral or azimuth resolution) of two rods when they can be distinguished in a plane perpendicular to beam propagation. The beam is not always rotationally symmetric, especially in sweeping ultrasound transducers (see chapter 11.1). In this case the lateral resolution is better in the sweeping direction than in the perpendicular direction (elevation resolution).

Further parameters are: contrast resolution (detectability of difference in density, see Figure 2.31.d), noise level.

Figure 2.31. Phantom body (a) to test diagnostic ultrasound devices. Radial (b) and lateral (c) resolution. Rods with different densities (d) to test sensitivity and contrast resolution.



4. Problems

1. Calculate the linearity error when an $R_p=10\text{ k}\Omega$ potentiometer is loaded with an $R_L=220\text{ k}\Omega$ resistor. It is enough to calculate the error in the middle position of the wiper ($\alpha = 0.5\alpha_M$), because this is the maximum error. Specify the error referenced to the maximum output voltage (%) and as absolute error (mV) when the supply voltage of the potentiometer is 5 V.
2. The wiper of the potentiometer is connected to a voltage follower to separate the load resistor as shown in Figure 2.32.a. This eliminates nonlinearity. Calculate the error caused by the common mode rejection ratio (CMRR = 80 dB), input offset voltage ($V_{0max} = 1\text{ mV}$), and input bias current ($I_{bmax} = 1\text{ nA}$) of the op amp.
3. A precision displacement transducer is built-up by a potentiometer with the following parameters:

- Useful displacement range: 200 mm
- Nominal resistance: $R_p=5\text{ k}\Omega$
- Temperature coefficient: $-200\text{ ppm}/^\circ\text{C}$

Linearity error: $\pm 0.05\%$. The error is caused by inhomogeneity it may show up anywhere on the displacement. The supply voltage is stable, +5 V. Calculate the minimal value of the load resistance to keep the nonlinearity error resulting only from load below 0.02 %. Calculate the maximum total nonlinearity error if the temperature change is 15°C during measurement.

4. The temperature dependence of the potentiometer does not cause error when the supply voltage is stable. The ratio of the output/supply voltage does not depend on temperature. The circuitry shown in Figure 2.32.b. generates + 5 V to the potentiometer (see problem 3) from the + 6 V supply voltage using R_s . The temperature coefficient of resistor R_s is $\pm 50\text{ ppm}$, negligible compared to the temperature coefficient of R_p . Calculate the maximum ΔV_{out} error when the wiper is in the uppermost position, provided $\Delta T=20^\circ\text{C}$.
5. Calculate the displacement belonging to the error voltages in problems 3 and 4.

6. Calculate the no-load voltage of the bridge circuit shown in Figure 2.5.c.
 7. The correct result of problem 6:

$$V_{\text{out}} = V_s \frac{R_{G2}R_{G3} - R_{G1}R_{G4}}{(R_{G1} + R_{G2})(R_{G3} + R_{G4})}$$

The expression can be simplified taking into account that the resistors of the bridge are nearly the same, thus they can be expressed as a base value and a small deviation:

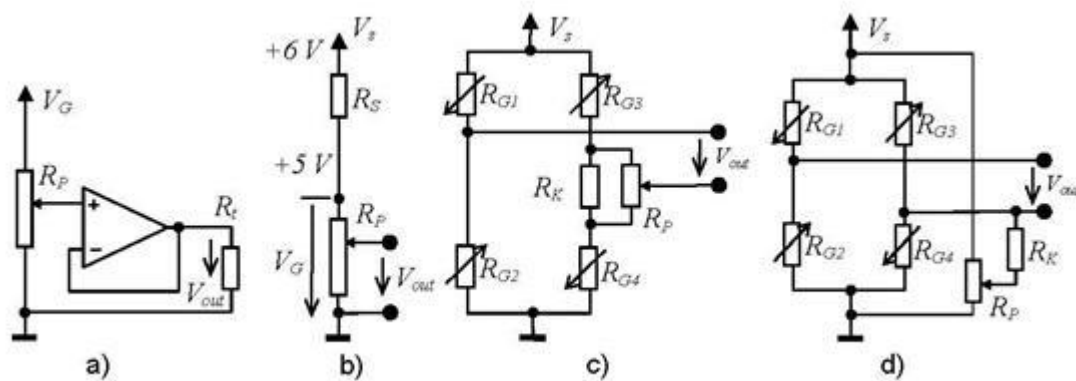
$$R_{Gi} = R_G + \Delta R_{Gi} \quad \text{where} \quad \Delta R_{Gi} \ll R_G$$

What are neglected to get the result below? Evaluate the neglected items.

$$V_{\text{out}} \cong \frac{V_s}{4} \left(\frac{\Delta R_{G2}}{R_G} + \frac{\Delta R_{G3}}{R_G} - \frac{\Delta R_{G1}}{R_G} - \frac{\Delta R_{G4}}{R_G} \right)$$

8. The circuitry shown in Figure 2.5.c has four strain gauges. Fixing can cause a deviation from the nominal value of R_G by $\pm 1\%$. As a result of the deviations the V_{out} output voltage of the bridge is not zero when there is no deformation. Figure 2.32.c shows a circuitry for zeroing. Calculate R_K so that the zero output voltage without deformation can be set by R_P even at worst-case deviations of R_{Gi} . $R_G = 120 \Omega$, $R_P = 1 \text{ k}\Omega$.
 9. The R_{G1} , R_{G4} strain gauges are stressed, R_{G2} , R_{G3} are compressed. The relative extension of the object is $\Delta l/l = 0.06\%$ at maximum stress. The supply voltage is $V_s = +6 \text{ V}$. The nominal values of strain gauges: $R_G = 350 \Omega$, $G = 2$. Calculate the maximal output voltage of the bridge after zeroing at no stress. Calculate the current consumption of the bridge.

Figure 2.32.



10. Calculate the necessary A_{us} symmetrical amplification of the amplifier connected to the output of the bridge in problem 9, if at maximum mechanical stress its output voltage is 2.5 V. Design a simple symmetrical amplifier with $R_{\text{ins}} = 100 \text{ k}\Omega$, using supply voltage is $\pm 6 \text{ V}$.
 11. Because of technical reasons we have to use the circuitry with two strain gauges shown in Figure 2.5.a. $V_s = 6 \text{ V}$, $R_G = 350 \Omega$, $G = 2$. R_{G1} is stressed, R_{G2} is passive. In the other branch of the bridge we use two precision resistors, $R_0 = 470 \Omega \pm 0.2\%$. Calculate the output voltage of the bridge at maximum mechanical stress ($\Delta l/l = 0.1\%$) provided the bridge was zeroed at no stress.
 12. The electrical power of the strain gauge must be limited to avoid error caused by self-heating. Calculate the maximum V_{smax} supply voltage that can be applied to the four strain gauge bridge if the strain gauges
 a. are small, their active surface is $1.5 \times 1 \text{ mm}$,
 b. are big, their active surface is $10 \times 5 \text{ mm}$.

The maximum allowed power on the active surface is 8 mW/mm^2 .

13. The parameters of a piezoresistive pressure sensor cell:

- Sensitivity: $\Delta p = 1 \text{ mmHg}$ causes $\Delta V_{ki}/V_s = 5 \mu\text{V/V}$
- Maximum pressure to be measured: $p_{\max} = 300 \text{ mmHg}$
- Maximum offset voltage at zero pressure equals $\pm 30 \text{ mmHg}$
- Sensor cell resistance: $R_G \approx 2400 \Omega$
- Suggested supply voltage: $V_s = 6 V_{\text{DC}}$

Calculate the symmetrical amplification to get 2.5 V output voltage at 250 mmHg pressure.

14. To zero the amplifier at $p = 0$ in problem 13 the circuitry in Figure 2.32.d is used. Calculate R_K so that by setting R_p potentiometer ($R_p = 470 \text{ k}\Omega$) to its terminal positions the maximum offset voltage can be cancelled.
15. We want to zero the bridge in problem 8 after A/D conversion. The useful output voltage of the bridge had to be calculated according to problem 9. We need a resolution better than 0.5 %. Calculate the necessary symmetrical amplification of the amplifier. Calculate the necessary resolution (number of bits) of the A/D converter.
16. The sensitivity of a piezoelectric vibration sensor is 0.5 pC/ms^{-2} , its frequency range is $0.1 \text{ Hz} \dots 16 \text{ kHz}$. The charge amplifier connected to the output of the sensor is in the 10 V/pC range, its output voltage is a 16 Hz frequency sine wave with $0.5 V_p$ amplitude. Calculate the mechanical vibration amplitude of the sensor.
17. A light sensor according to Figure 2.17.c. is used to measure the intensity of 560 nm wavelength yellow light of a LED. The sensitivity of the photodiode at this wavelength is 0.38 A/W . The LED has homogeneous beam, out of it an 0.3 mW power part reaches the sensor of the photodiode perpendicularly. Calculate the necessary R_{C2} to produce $V_{\text{out}} = 4 \text{ V}$ output voltage at this incident light. Calculate the error caused by the $V_o = 1 \text{ mV}$ offset voltage, and the $I_{\text{DS}} = 20 \text{ pA}$ dark current of the photodiode.
18. Calculate the attenuation of the intensity of an $f_0 = 2 \text{ MHz}$ frequency ultrasound while it propagates through a 10 cm fat tissue. Calculate the output intensity if the input intensity is $I_0 = 50 \text{ mW/cm}^2$.
19. The parallel ultrasound beam with $f_0 = 2 \text{ MHz}$ frequency propagates in fat tissue and reaches the boundary with liver tissue. Calculate the reflection. The thickness of fat tissue from the skin to the liver is 10 cm. Calculate the intensity of the reflected beam at the skin if the transmitted intensity is $I_0 = 50 \text{ mW/cm}^2$.
20. Blood flow is measured in a vessel close to body surface with a Doppler device, using $f_0 = 8 \text{ MHz}$ frequency ultrasound. The direction of the sensor and the vessel is at a 40° angle. Calculate the received frequency if blood flows towards the sensor with a 20 cm/s velocity. Calculate the frequency difference (Doppler frequency). Is it in the audible range?

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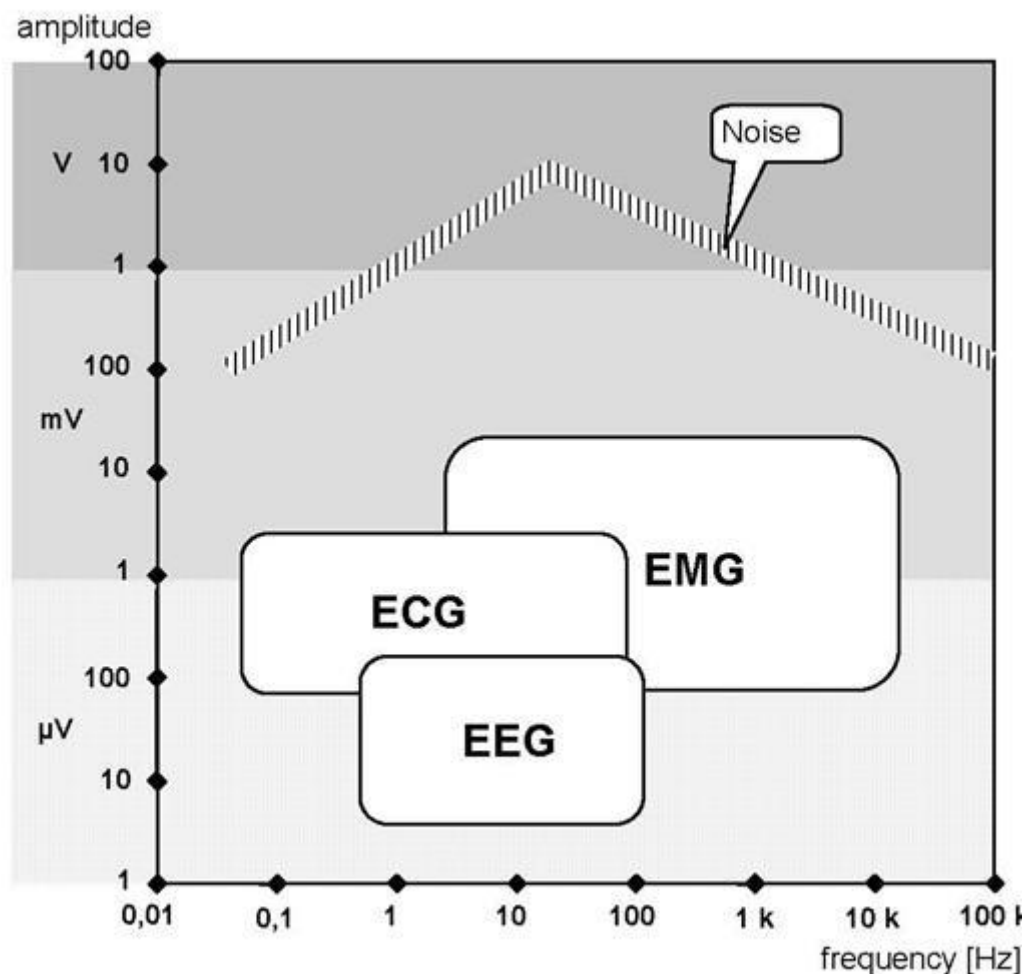
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Chapter 3. Biopotential amplifiers

1. Biopotentials and electrical noise

Biopotential is the result of physiological phenomena and can be measured between two electrodes attached to the body of a person. Usual amplitude- and voltage ranges are shown in Figure 3.1. The amplitude of superimposed noise is bigger by orders of magnitude making measurement of biopotentials a difficult task. The typical amplitude of superimposed noise is also given in Figure 3.1.

Figure 3.1. Typical amplitude of most frequently measured biopotentials and the superimposed noise as a function of frequency



ECG, EEG and EMG signals cannot be separated from each other and from superimposed noise based on their frequency range. The measurement method for separation must take into account a priori information about the source of the signals.

1.1. Equivalent circuits for signal- and noise sources

The most common source of noise is power line interference. Usually in the vicinity of a tested person there are big grounded surfaces (radiator, metal housing of instruments, conducting floor) and small surfaces at hot wire potentials (wire in the wall, AC power plugs, extension cords). Tested persons are not in direct connection with these surfaces but stray capacitance between them do exist (see Figure 3.2.a). The typical impedance of the

resultant capacitances at power line frequency is much higher than impedances between two points on the body of a person. As a result, while analysing the effect of noise sources, the body is considered to be equipotential, see Figure 3.2.b. The resultant capacitance to hot wire is C_L , the one to ground is C_G . Typical values: $C_L = 2\text{--}10$ pF, $C_G = 0.2\text{--}1$ nF. The two resultant capacitances form a voltage divider. Its input is power line voltage, its output is V_B , the voltage on the person's body. The body surface can be modelled by a voltage source with $V_B = 0.2 \dots 2$ V and output impedance calculated on the basis of the resultant capacitance $C_B = C_G + C_L$.

Figure 3.2. The body – environment capacitive coupling (a) and the equivalent circuit to model power line noise (b, c)

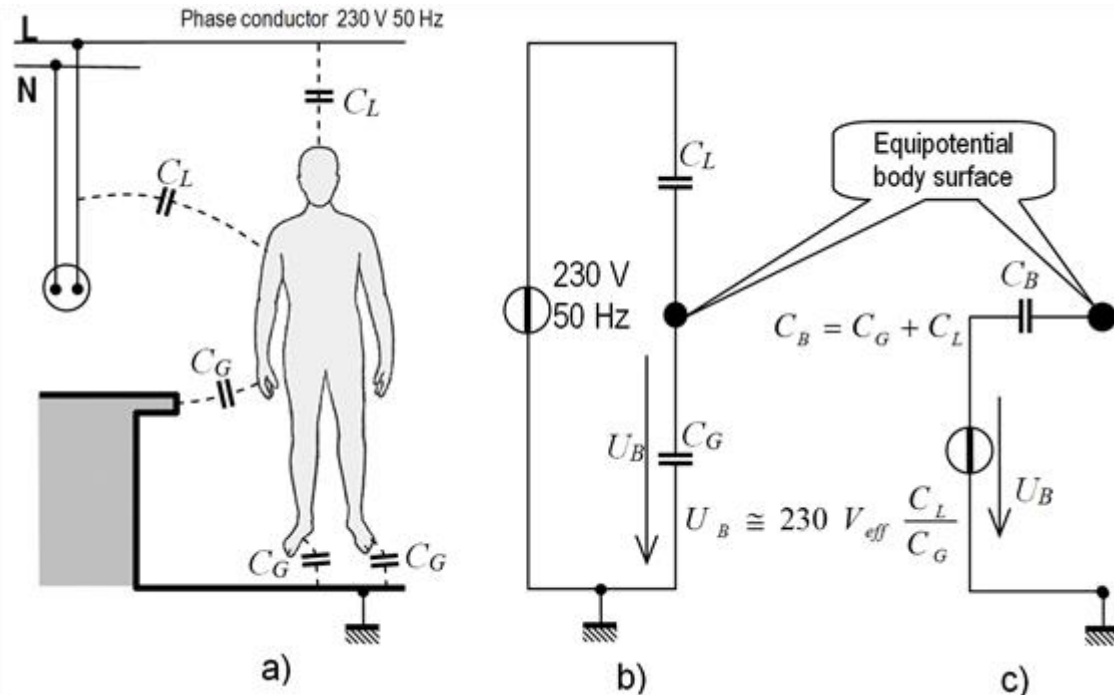
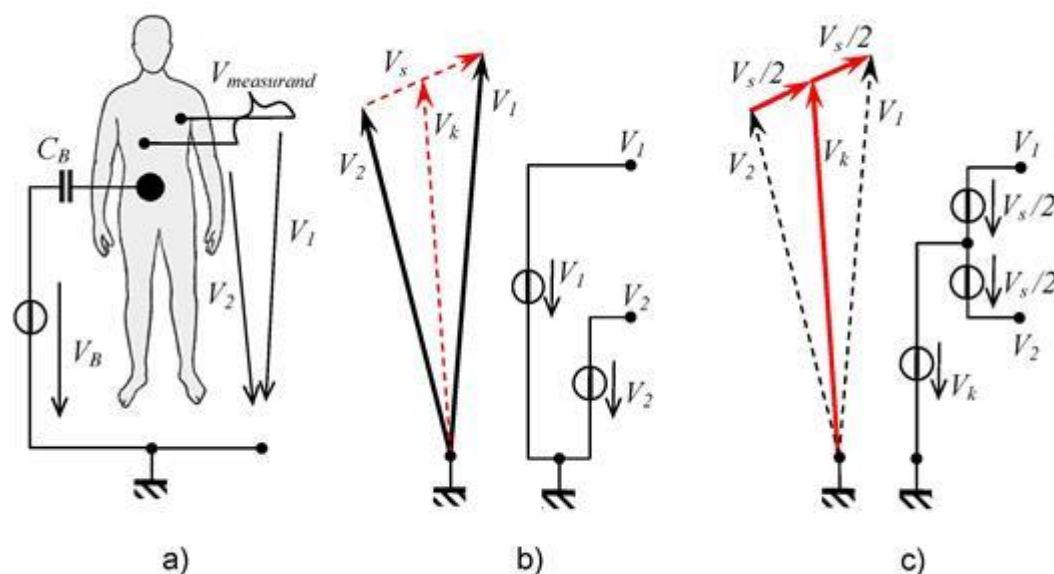


Figure 3.3. The biopotential to be measured and the modelled power line noise source (a), the equivalent circuit (b) and breaking down the voltage sources to symmetrical and common components (c)



Biopotential should be measured between points on the body while power line noise is present between the whole body surface and ground. The two points referenced to ground give voltages resulting from both the biopotential and power line noise. The measurement task is to determine the voltage difference of the two ungrounded points, see Figure 3.3. This is a general measurement task (not biopotential specific) the solution is to apply a symmetrical amplifier with three input terminals: two independent from ground.

The measurement task is illustrated in Figure 3.3.b showing the V_1 and V_2 voltages (vectors) and the equivalent V_s (symmetrical) and V_c (common) voltages (vectors). The biopotential to be measured is the symmetrical or differential voltage (see eq. 3.1.):

$$V_s = V_1 - V_2 \quad (3.1)$$

The potential difference (voltage vector) pointing from ground to the midpoint of V_s is the common voltage V_c , see eq. 3.2.

$$V_c = \frac{V_1 + V_2}{2} \quad (3.2)$$

Voltages V_1 and V_2 can be expressed with the symmetrical V_s and common V_c voltages:

$$V_1 = V_c + \frac{V_s}{2}, \quad V_2 = V_c - \frac{V_s}{2} \quad (3.3)$$

Figure 3.3.c shows the equivalent circuit according to equations 3.1. – 3.3. In Figure 3.3.c the symmetrical voltage is shown to be much bigger than usual compared to the common voltage. The reason is to make the symmetrical voltage visible. The amplifier should not amplify the common voltage with the same factor as the symmetrical voltage. It is not uncommon that on the body surface the biopotential is in the mV, power line noise in the V range. Biopotential is amplified by a factor of 1000 resulting in voltage around 1 V. The same gain for common voltage would require voltage around 1 kV and the amplifier would saturate!

1.2. Equivalent circuit of the body impedances

Impedances inside the body determine the resistance of the voltage source representing the biopotential. The input impedance of the amplifier must be much bigger than the resistance of the voltage source to be measured [3.4], [3.5], [3.6]. Driving sine wave current through the impedance its value can be determined by measuring its voltage, see Figure 3.4. The current level must be in the range that is safe for the person. Only the voltage with the same frequency as the excitation current is measured so noise currents with different frequency do not disturb the measurement. The impedance is calculated as given by eq. 3.4.

$$|Z_i| = \frac{U_{ieff}}{I_{Geff}} \quad (3.4)$$

The frequency dependent model of the impedance can be determined by measurements at different frequencies. The impedance between two electrodes attached to a person's body is the serial resultant of the resistance of the electrodes, the electrode-skin interfaces and the impedance within the body. If we want to model the impedance over a broad frequency range the equivalent circuit has to include several elements. The usual equivalent circuit with 2-3 R-C elements is adequate in the 0 – 10 kHz range.

Of the above described impedances connected in serial the biggest is the electrode-skin impedance. The resultant impedance hardly depends on the impedance within the body, i.e. on the distance between the two electrodes.

During safety analysis (see chapter 5.1) the impedances are supposed to be smaller than those in Figure 3.4. This increases safety. It is also true that impedance between two points on the body surface decreases when the voltage applied between them increases (e.g. dielectric breakdown of the skin). The wide range of usual impedances of humans is explained by different values of individuals. Furthermore, these impedances may change in time. Figure 3.5 shows a model of the biopotential to be measured the power line noise and the impedances present.

Figure 3.4. The resultant impedance between two electrodes on a person's body. The current paths and their cross sections between the electrodes (a) the serial resultant of impedances (b) and the frequency dependent equivalent circuit (c) that can be calculated by measurements using different frequencies.

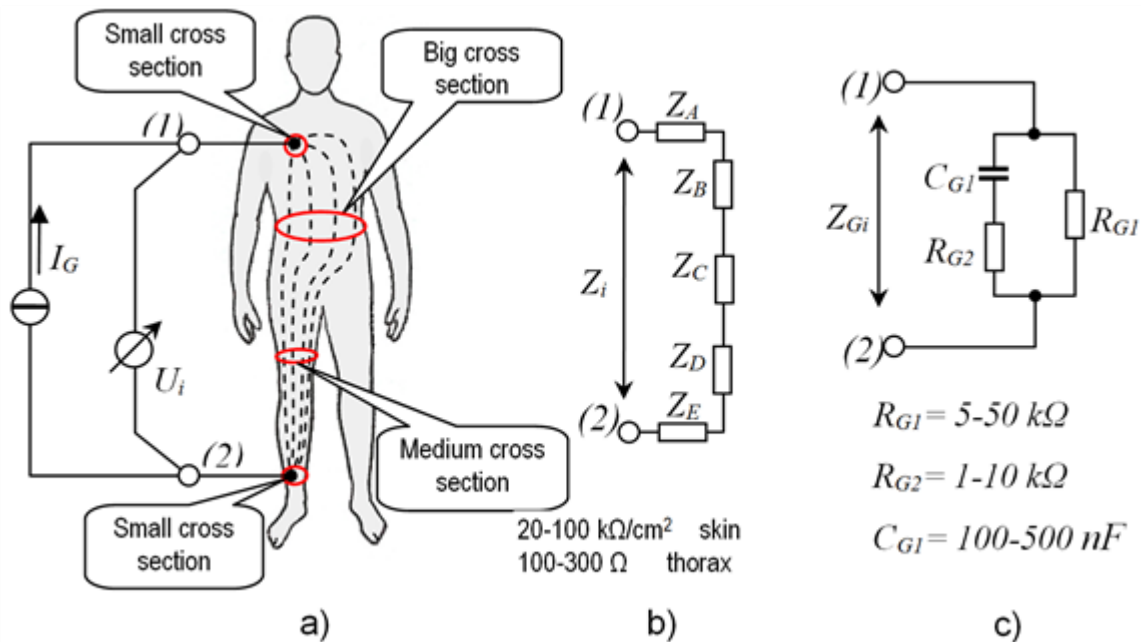


Figure 3.5. Equivalent circuit of the body taking into account the biopotential to be measured and the power line noise

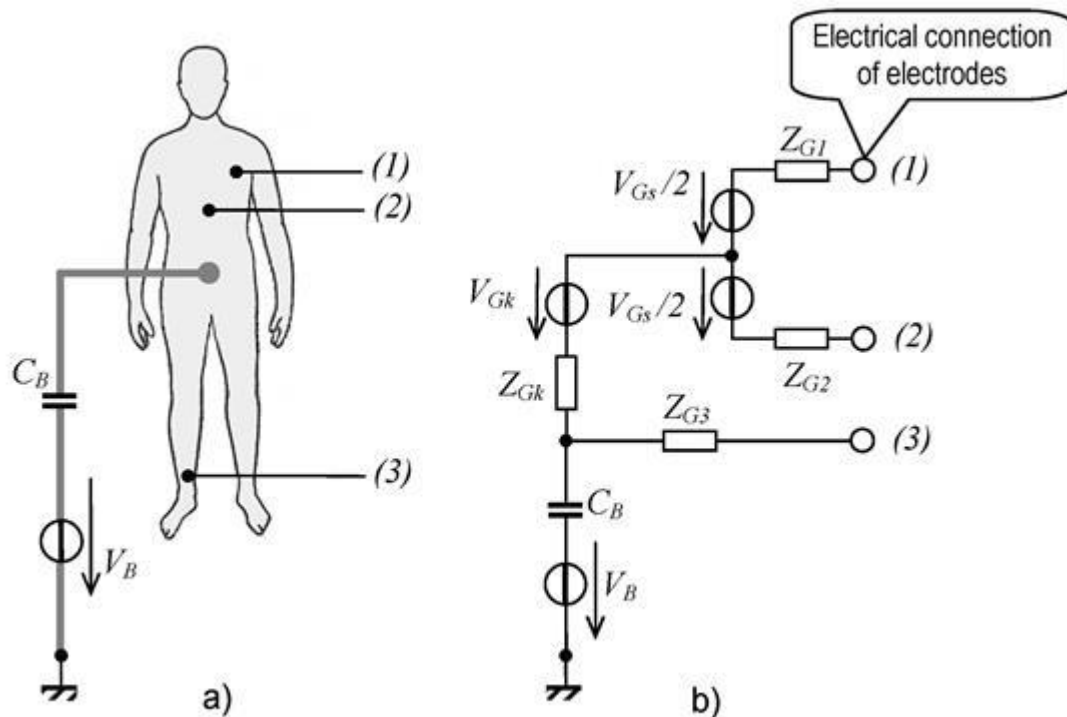


Figure 3.4.c shows that the impedances Z_{Gi} within the body are complex, depend on frequency. They are vector quantities characterized by complex numbers. The impedances have absolute value and phase. Z_G impedances

are not detailed in the equivalent circuit. The correct measurement circuit uses amplifiers with input impedances much bigger than body impedances. The body impedances – independent of their phase – are negligible compared to input impedance of biopotential amplifiers.

V_{Gk} can be an external (e.g. power line) noise, but can also be another biopotential we do not want to measure. While measuring EMG the person's ECG signal is noise. It is better to cancel the noise using appropriate measurement method than filter the sampled data during digital signal processing.

2. Symmetrical amplifiers

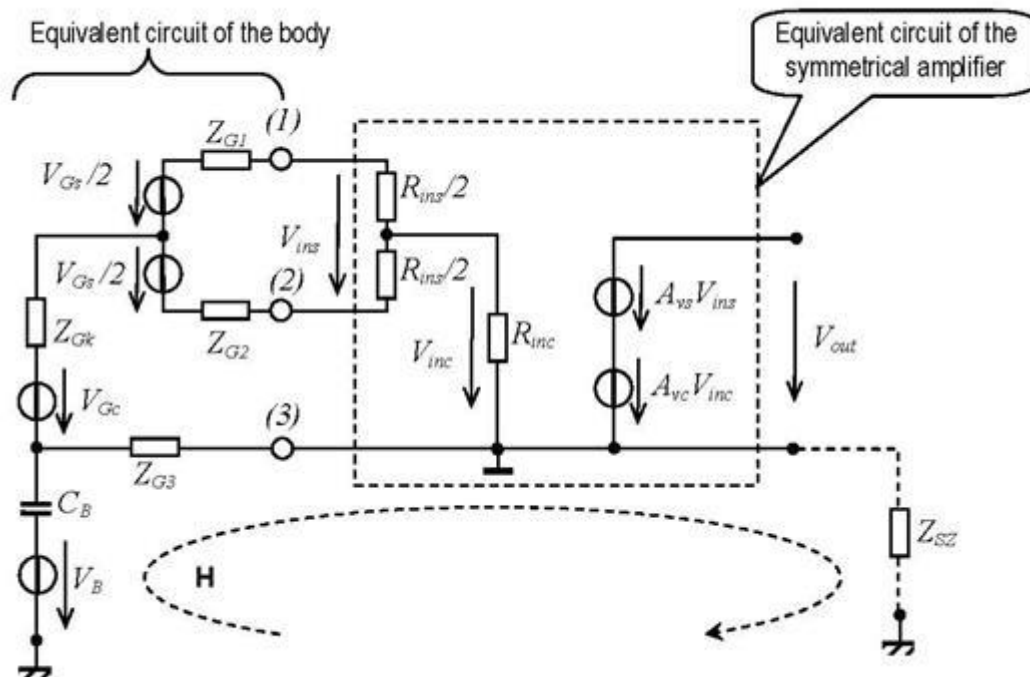
2.1. Equivalent circuit of the amplifier

Figure 3.6 shows the schematic of the symmetrical amplifier, the voltage to be measured and the noise to be suppressed. Without the structure of the amplifier its connections at the input and output are given showing the gain of symmetrical and common signals. The input of the amplifier is between points (1) and (2). (3) is a reference point both at the input and at the output, also called internal ground. All internal voltages are referenced to the internal ground, but it need not be connected to the ground in the wall outlet. The power supply of the amplifier is in connection with the internal ground.

In the schematic the output voltage is modelled with two controlled voltage sources. The voltage between input points (1) and (2) is the symmetrical input voltage V_{ins} , this is present at the output amplified by the symmetrical gain A_{vs} . The symmetrical input resistance is the resultant of the two identical resistors ($R_{ins}/2$) between the input points (1) and (2). A good estimation is that between the common point of the two $R_{ins}/2$ resistors and the internal ground is the common input voltage V_{inc} . (The estimation assumes that $R_{inc} \gg R_{ins}$.) The common input voltage amplified by the common gain A_{vc} is also present at the output. The total output voltage is given by eq. 3.5.

$$V_{out} = V_{ins}A_{vs} + V_{inc}A_{vc} \quad (3.5)$$

Figure 3.6. Schematic of the symmetrical amplifier, the voltage to be measured and the noise to be suppressed



V_{ins} is usually small, it has to be amplified. In some applications the gain is the resultant of two or more serial amplifier stages. The gain of the stages is often variable, the total gain may be as high as 10^6 . The common gain must be kept as low as possible ($|A_{vc}| < 1$), in the ideal case $A_{vc} = 0$. The common mode rejection ratio (CMRR) is the ratio of the symmetrical and common gain; see eq. 3.6. Often CMRR is given instead of A_{vc} .

$$CMRR = \frac{A_{vs}}{A_{vc}} \quad (3.6)$$

CMRR must be high to separate biopotential from noise. In case of ECG the potential to be measured (symmetrical voltage) is in the mV range while power line noise (common voltage) is in the V range.

Typical values for biopotential amplifiers: $|CMRR| = 10^5 \dots 10^6$, in logarithmic scale: 100 ... 120 dB.

(There are other schematics for symmetrical amplifiers. The input resistances can be in delta circuit instead of the star used in Figure 3.6. The two circuits can be transformed into each other. Common voltage gain can be modelled with an input generator, too.)

Input impedances also have an effect on measurement accuracy of biopotentials. The generator impedance (see Figure 3.4) is varying and we cannot influence its value. To assure $V_{ins} = V_{Gs}$ at the input of the amplifier independent of the varying generator impedance R_{ins} must be much higher than the absolute value of $Z_{G1} + Z_{G2}$ (usually $R_{ins} > 2.5 \text{ M}\Omega$).

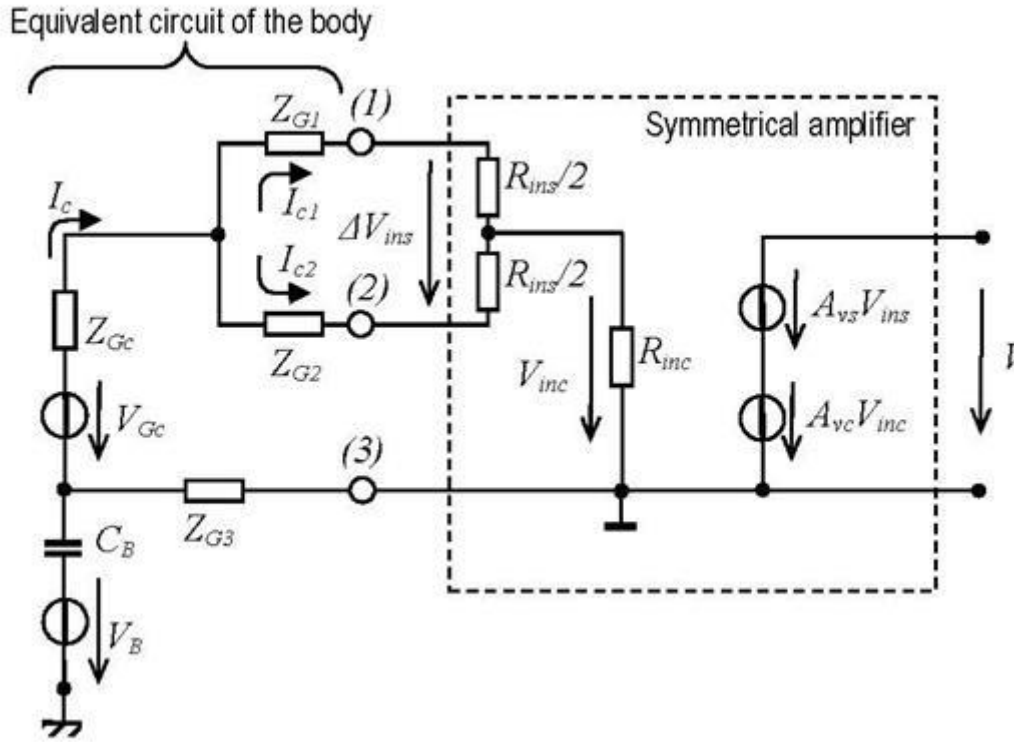
In linear systems we can apply the *theory of superposition*. Only one generator is supposed to be active at a time, all other voltage sources are substituted by short circuits, all other current sources are substituted by open circuits. The voltage between two points is calculated as a sum of voltages calculated so that always a single generator is active.

The body surface of the person is not grounded. Amplifiers need galvanic connection between their input points (1), (2) and internal reference point (3). (The 10 pA ... 10 nA input bias current of the amplifier needs this connection.) The internal reference (3) is connected to the body of the person so that the galvanic connection is present through the body and it does not disturb the biopotential to be measured. Seemingly the V_B noise voltage does not affect the input voltage of the amplifier. The output of the amplifier is connected to other circuits the internal ground of which is in (mainly capacitive) connection with the ground in the wall outlet. This connection is modelled with Z_M . A loop is formed (**H**) in which noise current flows through the impedance Z_{G3} and produces a noise voltage across it. The amplifier senses this noise voltage as an increase of V_{Gc} . The smaller are the impedances in the loop compared to Z_{G3} the bigger part of V_B falls Z_{G3} . This requires that the connected circuits have high impedance to wall outlet ground. (See also section 3.6.) Further problem is that in series with Z_M a noise voltage source can be present. Ungrounded devices – similarly to ungrounded persons – always have stray capacitances to the hot and ground wire of power line resulting in a noise voltage similar to V_B . In case of grounded devices the not completely equipotential grounding causes noise voltage. (See also chapter 3.3.3.)

2.2. Resultant common mode rejection

Above it was shown that accurate measurement of V_{Gs} biopotential requires big R_{ins} . It is also important that common noise voltage V_{Gc} cause potential difference as small as possible between input points (1) and (2). This error is shown in Figure 3.7.

Figure 3.7. V_{Gc} causes symmetrical error voltage when generator impedances do not match



As a result of V_{Gc} I_c current flows in the loop as shown in Figure 3.7. I_c is divided into I_{c1} and I_{c2} the two currents flowing through Z_{G1} and Z_{G2} . I_{c1} and I_{c2} are nearly equal because the I_c current division ratio is determined by the $R_{ins}/2$ resistors, see eq. 3.7 and 3.8.

$$I_{c1} \cong I_{c2} \cong \frac{I_c}{2}, \text{ because} \quad (3.7)$$

$$\frac{R_{ins}}{2} \gg Z_{Gi}, \quad i = 1, 2 \quad (3.8)$$

If Z_{G1} and Z_{G2} are not equal then they cause a ΔV_{ins} error voltage between input points (1) and (2) which cannot be differentiated from the biopotential to be measured, V_{Gs} , see eq. 3.9.

$$\Delta V_{ins} = I_{c2} Z_{G2} - I_{c1} Z_{G1} \cong \frac{I_c}{2} \Delta Z_G \quad (3.9)$$

where

$$I_c \cong \frac{V_{Gc}}{Z_{G3} + Z_{Gk} + \frac{R_{ins}}{4} + R_{inc}} \approx \frac{V_{Gc}}{R_{inc}} \text{ and} \quad (3.10)$$

$$\Delta Z_G = Z_{G2} - Z_{G1} \quad (3.11)$$

This error can effectively be decreased by decreasing current I_c by increasing the common input impedance of the amplifier. (The difference of Z_{G1} , Z_{G2} remains mainly out of control.)

$$\Delta V_{ins} \approx \frac{V_{inc}}{2R_{inc}} \Delta Z_G \quad (3.12)$$

Eq. 3.12 takes into account that as a result of the big R_{inc} $V_{inc} \approx V_{Gc}$. The error is characterized by the $CMRR_{imbalance}$, see eq. 3.13.

$$CMRR_{\text{imbalance}} = \frac{V_{\text{inc}}}{\Delta V_{\text{ins}}} = \frac{2R_{\text{inc}}}{\Delta Z_G} \quad (3.13)$$

The resultant common mode rejection is determined by the CMRR of the symmetrical amplifier (CMRR) and the imbalance; see eq. 3.14.

$$\frac{1}{CMRR_{\text{resultant}}} = \frac{1}{CMRR_{\text{imbalance}}} + \frac{1}{CMRR} \quad (3.14)$$

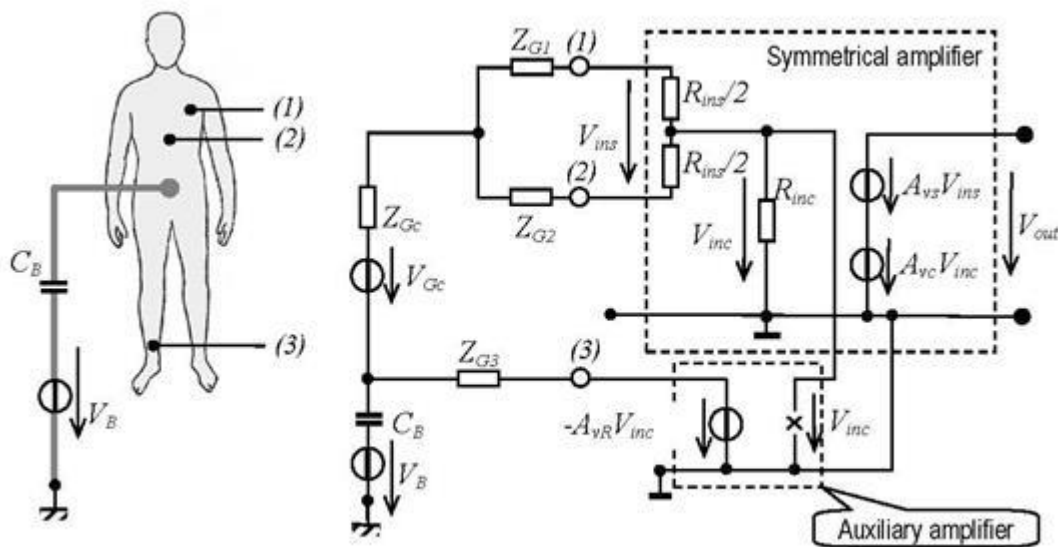
The sign of the components is ambiguous. We get the worst case if the absolute values of the minimal CMRRs are taken, see eq. 3.15.

$$\frac{1}{CMRR_{\text{resultant}}} = \frac{1}{|CMRR_{\text{imbalance min}}|} + \frac{1}{|CMRR_{\text{min}}|} \quad (3.15)$$

The resultant CMRR can only be high if both components are high. This means both symmetrical and common input impedances must be high, $R_{in} > 2,5 \text{ M}\Omega$ $R_{in} > 1 \text{ G}\Omega$. Biopotentials to be measured are always alternating signals DC coupling would not be needed. Amplifiers require galvanic connection also the imbalance (see Figure 3.7) can be kept low with DC coupling. The next – asymmetrical – stage following the symmetrical amplifier can use AC coupling. The maximal voltage swing of the amplifier must not be exceeded in order to be in the linear range. For nearly all operational amplifiers this is less than the power supply. If the voltage inside the amplifier should be bigger than distortion will happen. It is common that biopotential amplifiers are battery operated requiring small power consumption. This results in small supply voltages (2.7...5 V). We need symmetrical amplifiers that have high CMRR and keep common voltage amplitude at a maximum 1...2 V.

2.3. Actively decreasing common voltage

Figure 3.8. The Driven Right Leg (DRL) technique. Schematic of the loop to compensate V_{Gc} showing the auxiliary amplifier.



The common voltage at the input of the symmetrical amplifier can be decreased by connecting electrode (3) to the output of an auxiliary amplifier (see Figure 3.8). The auxiliary amplifier can decrease the common voltage by producing a voltage adverse to the original common voltage. In Figure 3.8 the auxiliary amplifier is controlled by the V_{inc} voltage of the symmetrical amplifier. In ECG measurement electrodes are attached to three limbs (right arm, left arm, left leg) to measure electrical activity of the heart (see chapter 6). The fourth limb, the right leg was available for active potential driving; hence the technique shown in Figure 3.8 is called Driven Right Leg (DRL) technique.

The auxiliary amplifier realizes negative feedback for the common voltage. Suppose that R_{inc} is much bigger than the serial resultant of $Z_{G3} + Z_{Gc}$ + parallel resultant of the two $Z_{Gi} + R_{ins}/2$ branches. In this case the output voltage of the auxiliary amplifier (3) is only slightly divided to produce V_{inc} common voltage at the input of the symmetrical amplifier. For the loop auxiliary amplifier – body – input of symmetrical amplifier we can write (see eq. 3.16):

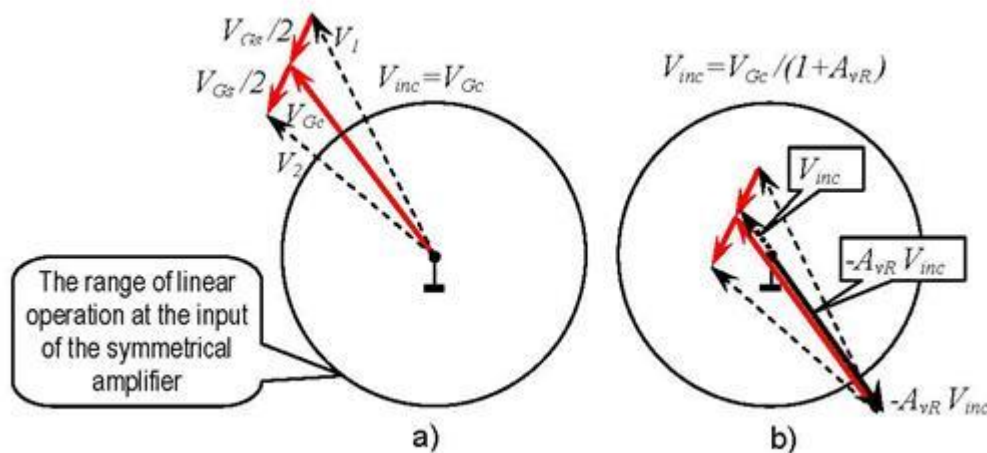
$$-A_{vR}V_{inc} + V_{Gc} = V_{inc} \quad (3.16)$$

Expressing V_{inc} (see eq. 3.17):

$$V_{inc} = \frac{V_{Gc}}{1 + A_{vR}} \quad (3.17)$$

The auxiliary amplifier (gain is A_{vR}) decreases V_{inc} compared to V_{Gc} , see Figure 3.9. Voltages are shown as vectors. The symmetrical amplifier saturates (unable to produce the voltage it should according to the input voltage) when the common input voltage is too big (Figure 3.9.a). The auxiliary amplifier partly compensates the common input voltage thus the symmetrical amplifier is able to produce voltage according to its input voltage. The auxiliary amplifier also increases the CMRR by decreasing the common input voltage. In the feedback loop of the auxiliary amplifier there are elements that are beyond control of the circuit designer (stray capacitances, patient's impedances). The stability of the feedback must be assured for worst-case situation by analysing the given application. As a general rule, the feedback loop remains stable if the gain of the auxiliary amplifier does not exceed $\times 100$ (40 dB). When ECG is measured using limb electrodes then the body surface is driven by an electrode on the right leg because it is not needed for the standard leads. This explains the name 'Driven Right Leg', DRL [3.7].

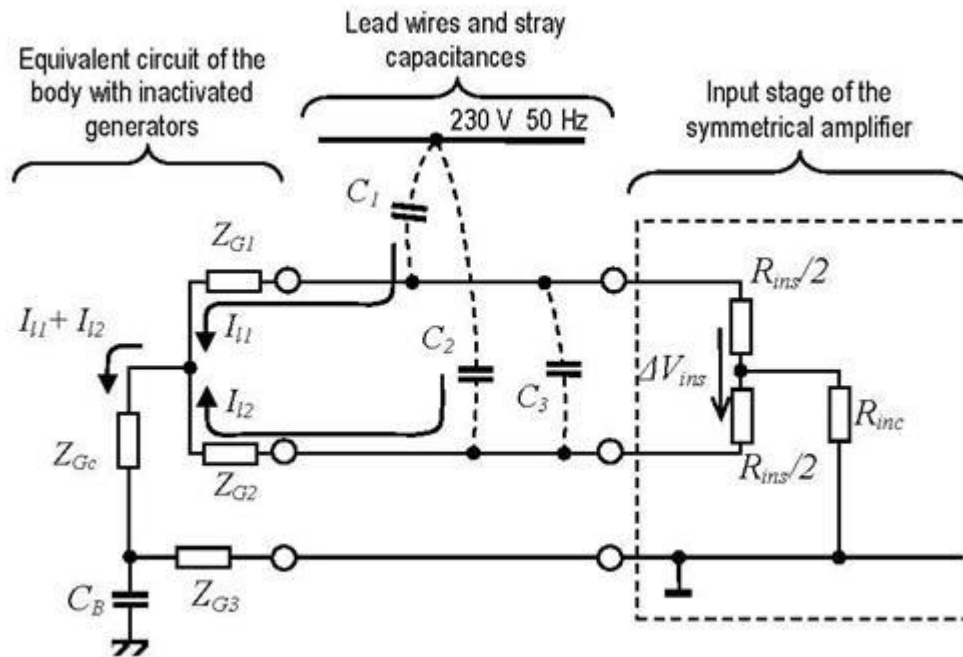
Figure 3.9. V_{inc} is too big for the symmetrical amplifier (a). The auxiliary amplifier decreases the common voltage (b).



3. Noise signals through cables

3.1. Capacitive coupled noise

Figure 3.10. Stray capacitances between power line and cables



There are stray capacitances between hot wires (and other metal surfaces on the same potential) and cables connecting electrodes to devices (see Figure 3.10). Through stray capacitances C_1 and C_2 (values 1 ... 10 pF) the power line results in leakage currents I_{I1} and I_{I2} flowing towards the person's body (Z_G impedances can be neglected compared to the input impedance of the amplifier). The voltage difference across Z_{G1} and Z_{G2} impedances a voltage difference will be present at the input of the amplifier, see eq. 3.18.

$$\Delta V_{ins} = I_{I1}Z_{G1} - I_{I2}Z_{G2} \quad (3.18)$$

The capacitance between the cables (C_3) in itself does not cause error voltage but connected in parallel decreases the symmetrical input impedance.

Shielded cable (see Figure 3.11) protects against the effect of stray capacitances. Shielding must be connected to a potential that helps I_i currents not to flow across Z_{G1} and Z_{G2} impedances. Nevertheless, within shielding C_4 and C_5 cable capacitances are present ($C = 100...200$ pF/m). These capacitances are much larger than stray capacitances and can lead in error voltage, too. If shielding is connected to a noisy point, then the noise voltage will be transferred to the heart of the cable. Potential difference between shields causes symmetrical error voltage, as a rule, shields must be connected to a single point.

Figure 3.11. Shielding connected to the inner ground leads off noise current from the inputs but increases capacitances

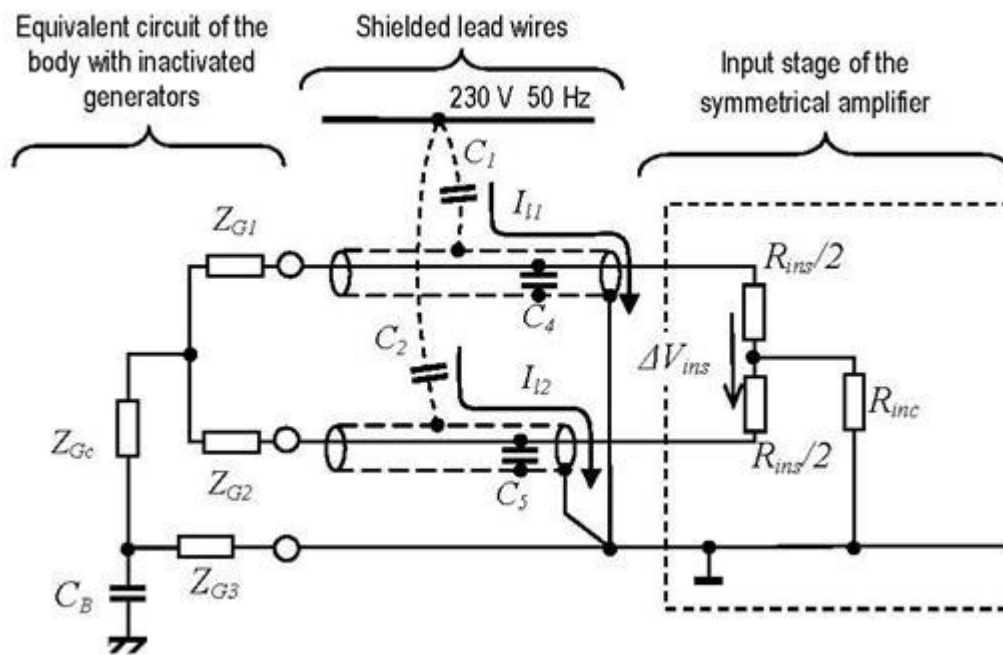
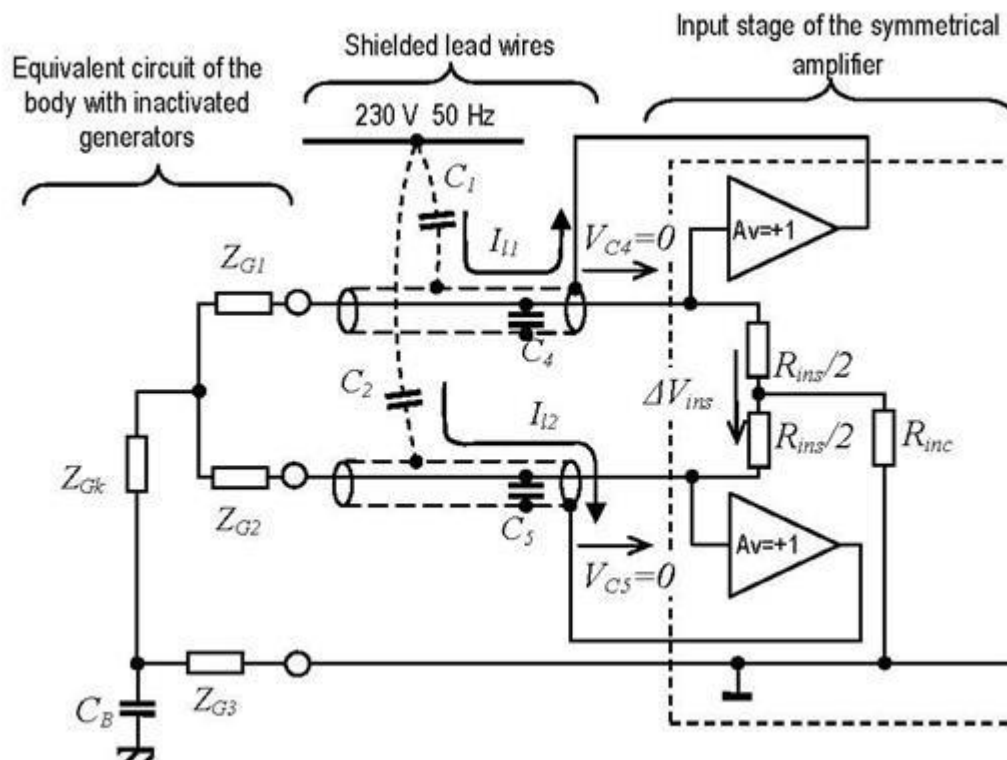


Figure 3.12. Voltage bootstrap cancels the capacitance increasing effect of shielding



Voltage bootstrap can cancel the effect of the capacitance, see Figure 3.12. A voltage follower drives the potential of the shield to be equal to the potential of the heart of the cable. The current of C_1 and C_2 flows through the output of the voltage followers (to the internal ground). Voltage followers have high input impedance so it does not decrease the input impedance of the symmetrical amplifier. As the potential of the

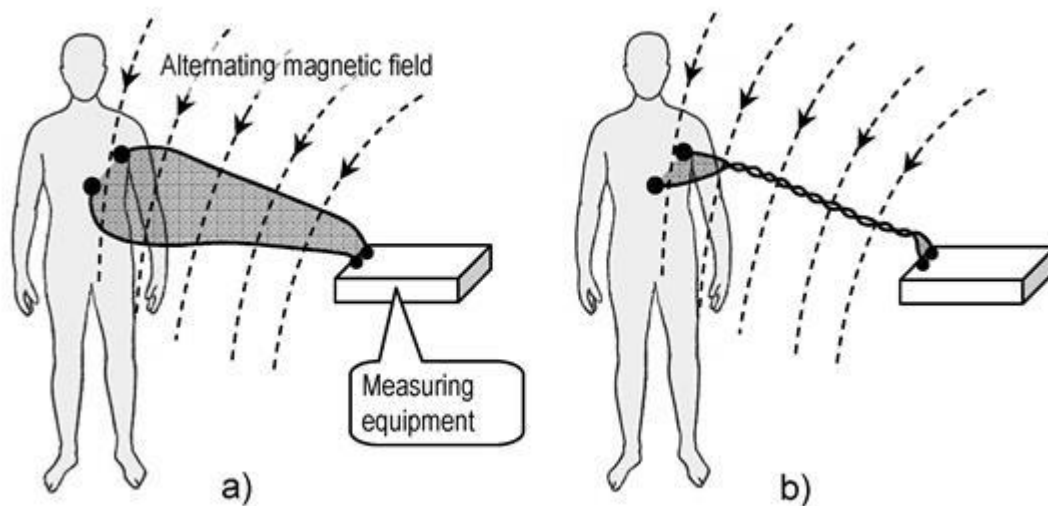
shield changes together with the potential of the heart of the cable, the voltage across capacitances C_1 and C_2 are zero ($V_{C4} = 0$, $V_{C5} = 0$). As a result, C_4 and C_5 capacitances act as if their value was zero.

The voltage follower has a nominal gain of +1. The amplifier is part of a feedback loop, the loop gain must be set below 1 to avoid oscillation. Usually a voltage divider at the output of the voltage follower sets the loop gain to 0.98 ... 0.99.

3.2. Inductively coupled noise

The current of equipment drawn from the power line in the vicinity of persons induces alternating magnetic field. Cables from the person to the device form a loop in which the magnetic flux Φ_l induces voltage. This voltage appears as an error voltage in series with the symmetrical voltage to be measured. The error can be decreased by decreasing the area of the loop. This can be achieved by twisting the cables (see Figure 3.13). Simple shielded cable does not protect against magnetic induction.

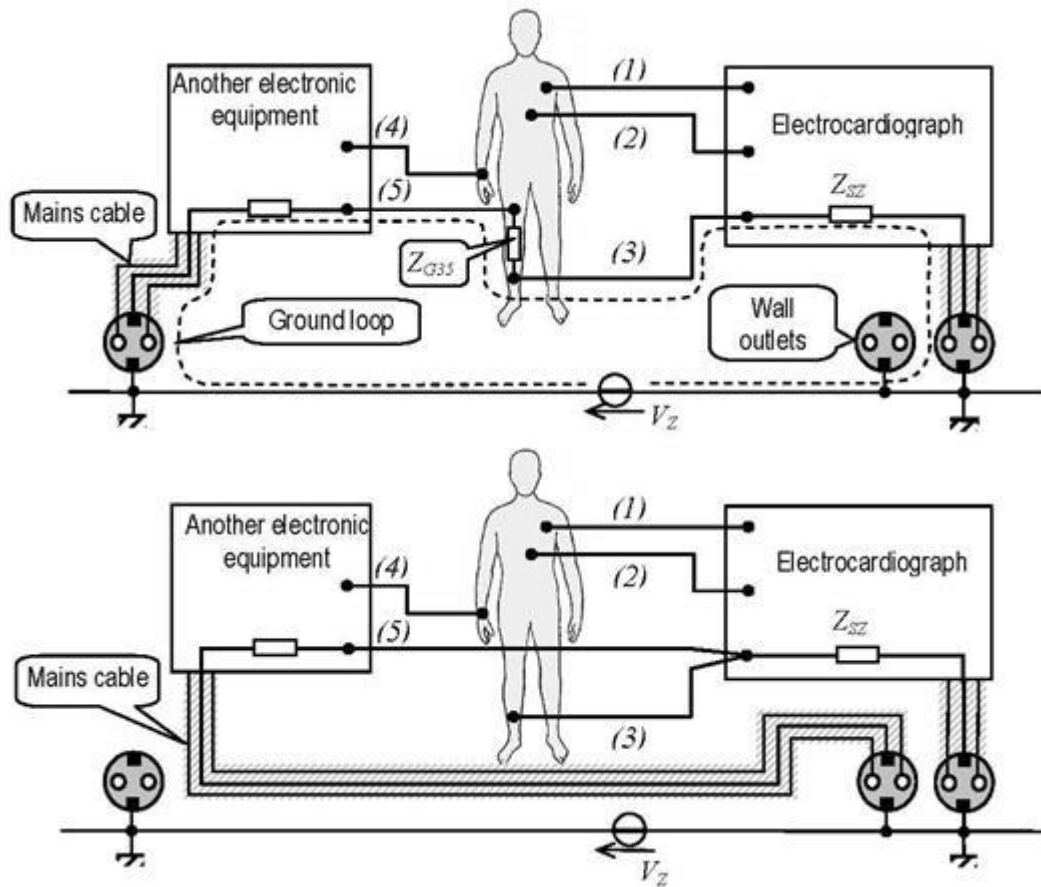
Figure 3.13. Decreasing the magnetic induction of noise by twisting the cables



3.3. Ground loop

The power line connector contains three wires: hot, neutral and ground. Earth ground serves as safety ground. (In laboratories a grounding loop for measurement is sometimes formed.) Grounding loops have small impedance and are theoretically equipotential. In practical cases in between two points of the grounding loop several hundred millivolts can be present. This might cause substantial error if it gets into the measuring circuit. The potential difference along the grounding loop temporarily might even be higher if a failure exists in one of the connecting devices. The upper drawing in Figure 3.14. shows two biomedical devices connected to the same person. There is a potential difference V_n between the earth grounds of the two wall outlets. The majority of V_n will be across the body because it has the highest impedance in the loop. This noise voltage may appear as common or as symmetrical input voltage. In the lower drawing of Figure 3.14. the two devices are connected to wall outlets close to each other thus there is no potential difference between their earth ground points. Notice that the reference connections (3) and (5) are connected to each other directly (grounding to a single point); there is no current path in the body between them. The configuration in the lower drawing in Figure 3.14 avoids noise current path in the body. Should there be further electronic devices connected to the person the configuration of grounding might become ambiguous. The solution is that devices in connection with humans must be isolated from the power line with high impedance. This is advantageous for safety reasons and for keeping power line noise low. Even in this case the devices must be connected to wall outlets close to each other and their reference inputs must be connected to a single point.

Figure 3.14. The ground loop (upper drawing) and its elimination using wall outlets close to each other and connecting the reference inputs of devices to a single point (lower drawing)



4. Symmetrical amplifiers

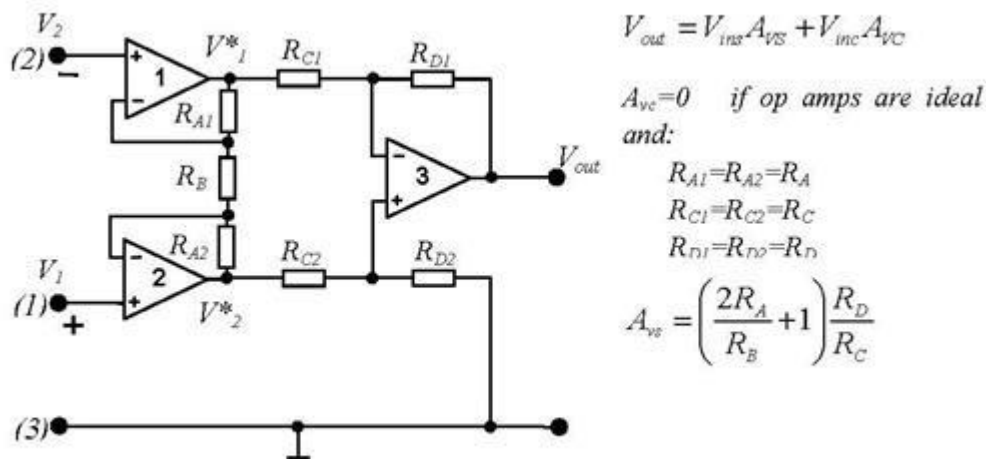
There are many different circuit schematics for symmetrical amplifiers. Most of them are realized using operational amplifiers (op amps) that are symmetrical amplifiers themselves. The necessary precise gain needs to add feedback loop to op amps. Measurement of biopotentials needs high input impedances (both symmetrical and common). The highest input impedance is achievable if there are no resistors (only those for overvoltage protection) between the input and the input of the operational amplifier [3.8], [3.9].

4.1. Instrumentation amplifier with three op amps

The name instrumentation amplifier reflects that the circuit is a symmetrical amplifier with a high precision gain, high CMRR and high input impedance. The circuit schematic is given in Figure 3.15.

The resultant CMRR of the circuit depends on the CMRR of the op amps and the precision of the resistors: how small is their deviation from the nominal value. The matching can be assured by applying high precision resistors or by trimming one of them. Using 0.5 % tolerance resistors and general purpose op amps the resultant CMRR without trimming is 60 ... 80 dB up to frequencies 0.5 ... 5 kHz. The resultant CMRR gets worse as frequency increases. The three op amp instrumentation amplifier is available packaged in one chip with the possibility to set the gain A_{vs} with an external resistor R_B .

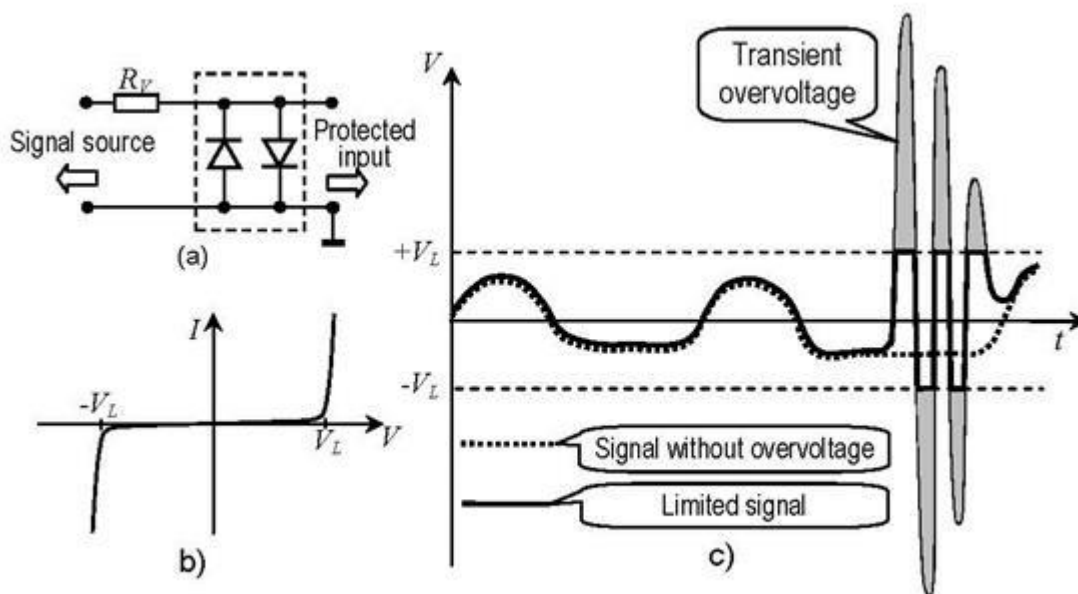
Figure 3.15. Three op amp instrumentation amplifier



4.2. Input protection of bioamplifiers

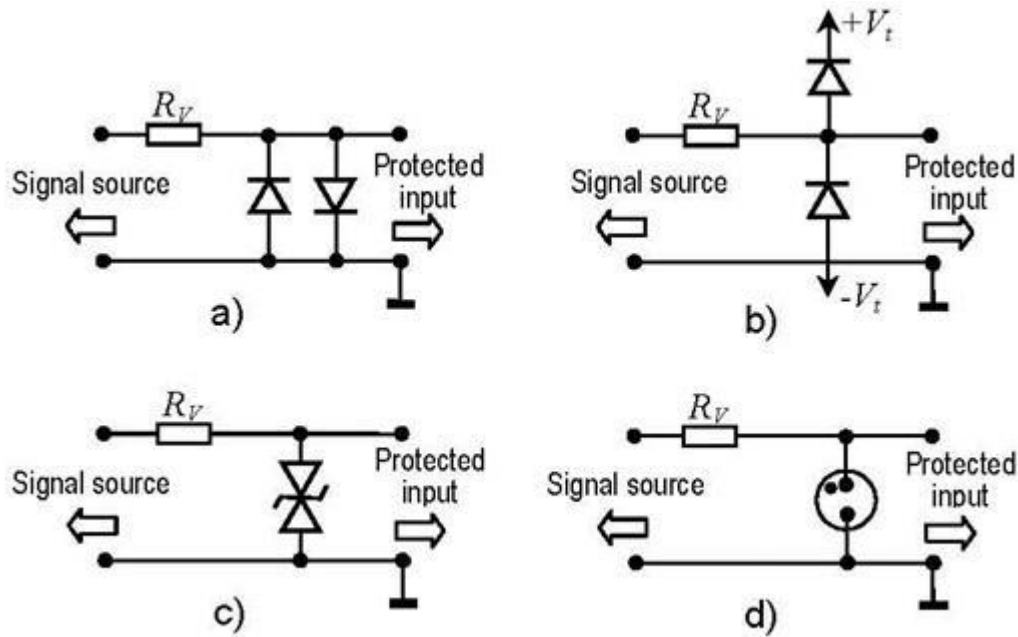
Voltage pulses can be present at the input with amplitudes much bigger than those to be measured. Static discharge (person charged during movement touches the input), disconnecting and reconnecting connecting cable during power on, lightning nearby, application of a defibrillator can result in high voltage peaks that can break down the amplifier [3.10]. Overload protection must not influence normal operation. The smallest voltage limit can be set as shown in Figure 3.16.a. The two antiparallel diodes have very high impedance while the voltage across them is lower than a given V_L limit. Should the voltage want to be higher than V_L one of the diodes start leading current and its voltage hardly increases above V_L (see Figure 3.16.b). Current has to be limited with a serial resistor ($R_V = 200 \dots 500 \text{ k}\Omega$) to protect both the person and the amplifier. While the diodes limit the input voltage the signal is distorted (Figure 3.16.c) but the amplifier is protected. The energy of the overvoltage (in the figure the area shown in grey) must be dissipated by the protecting circuit.

Figure 3.16. Overload protection circuit with diodes (a), the voltage-current characteristic of the framed section (b), the effect of protection on the signal to be measured (c)



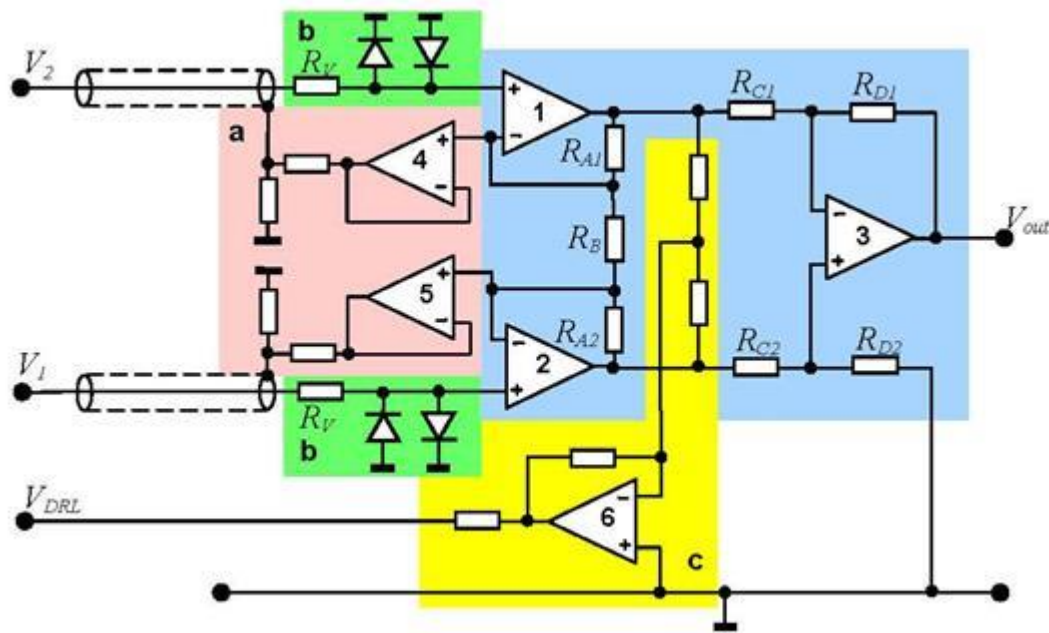
The usual overload protecting nonlinear elements are given in Figure 3.17. The protecting circuit connected to the high input impedance amplifier must have a high input impedance itself while $|V_{in}| < V_L$. The diode has high impedance around zero voltage if its reverse current is small (10 ... 100 pA).

Figure 3.17. Overload protecting circuits. Diodes with small reverse current between input and ground limit the input voltage to $V_L = 0.6 \dots 1.1$ V (a). Diodes with small reverse current between input and power supply limit the input voltage to $V_L = V_t + 1.1$ V (b). Zener diode limits the voltage according to its nominal voltage, $V_L = 3 \dots 30$ V. Gas discharge tube has $V_L = 70 \dots 90$ V (d).



Integrated amplifiers have built-in overload protection but these have limited performance. Transients with high energy demand the application of two or more protecting circuits in series. A complex input stage is shown in Figure 3.18.

Figure 3.18. A complex biopotential amplifier with bootstrapped shielding (a), overload protection (b) and driven right leg auxiliary amplifier (c)



4.3. Internal noise sources of amplifiers

By appropriate termination of the input neither signal nor external noise get into the amplifier. Even in this case – especially when its gain is high – at the output of the amplifier noise signal is present. This noise is always present and adds up to the measured biopotential. Main sources of such noise are:

1. Power supply noise either generated by the power supply unit (e.g. switching unit) or it originates from the mains and gets through the unit. Bypassing, decoupling and appropriate grounding can keep power supply noise low.
2. External noise that gets into the amplifier through radiation or via parasitic and stray components (see chapter 5.5). Shielding and RF filtering is needed to cancel this type of noise.
3. Internal noise. Resistors and semiconductors have inherent noise generators. Appropriate circuit schematic and good quality components help keep this type of noise low. The above two noise types usually have characteristic frequency while internal noise is mainly white noise (stochastic and wideband). All cascaded stages in an amplifier have internal noise. Usually the noise of the input stage dominates because it is amplified by all further stages. The bandwidth of the amplifier should be limited to correspond to the biopotential to be measured. Wider bandwidth decreases the signal/noise ratio.

5. Multichannel amplifiers

Body surface potential mapping often uses more than hundred electrodes. Such applications require many channels with uniform parameters. One possible solution – where further channels can easily be added – is given in Figure 3.19 [3.11]. An average potential will be present on the K wire which can be regarded as common voltage, see eq. 3.19-3.21.

$$\sum_{i=0}^n I_i = 0, \quad (3.19)$$

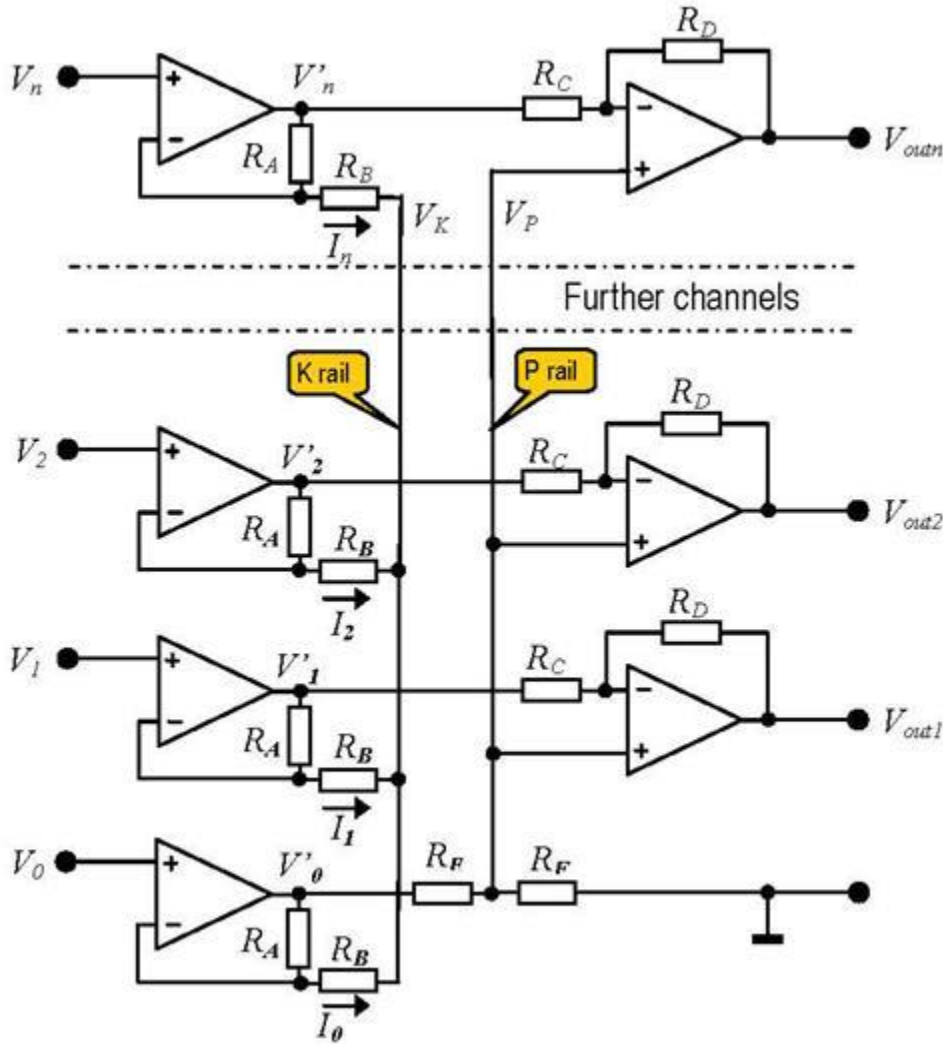
$$\sum_{i=0}^n \frac{V_i - V_c}{R_B} = 0, \quad (3.20)$$

$$V_c = \frac{\sum_{i=0}^n V_i}{(n+1)} \quad (3.21)$$

The vector diagram in Figure 3.20.a shows that potential V_k is the centroid of the n input potentials. Making use of V_k for all channels the output voltage of the first stage is given by eq. 3.22.

$$V'_i = V_i \frac{R_A + R_B}{R_B} - V_c \frac{R_A}{R_B} \quad (3.22)$$

Figure 3.19. Multichannel amplifier structure



The first stage of each channel amplifies the difference between the input voltage V_i and V_k thus relatively high gain can be set without saturating the stage. V_k can be used for driving the body potential (like driven right leg).

Channel 0 is decisive because the input voltage of all other channels will be referenced to V_0 , see eq. 3.23.

$$V'_0 = V_0 \frac{R_A + R_B}{R_B} - V_c \frac{R_A}{R_B} \quad (3.23)$$

The R_E , R_F voltage divider generates V_P voltage from to wire P, see eq. 3.24.

$$V_P = V'_0 \frac{R_F}{R_B + R_F} \quad (3.24)$$

The output voltage of channels 1 ... n is given by eq. 3.25.

$$V_{out\ i} = -V'_i \frac{R_D}{R_C} + V_p \frac{R_C + R_D}{R_C} = -V'_i \frac{R_D}{R_C} + V'_0 \frac{R_F}{R_E + R_F} \frac{R_C + R_D}{R_C} \quad (3.25)$$

The output voltage of a channel is proportional to $V_0 - V_i$ if the ratio of resistors R_C , R_D , R_E and R_F agrees with eq. 3.26.

$$\frac{R_D}{R_C} = \frac{R_F}{R_E + R_F} \frac{R_C + R_D}{R_C} \quad (3.26)$$

Simplifying the condition:

$$\frac{R_C}{R_D} = \frac{R_E}{R_F} \quad (3.27)$$

When eq. 3.27 is true:

$$V_{out\ i} = (V'_0 - V'_i) \frac{R_D}{R_C} \quad (3.28)$$

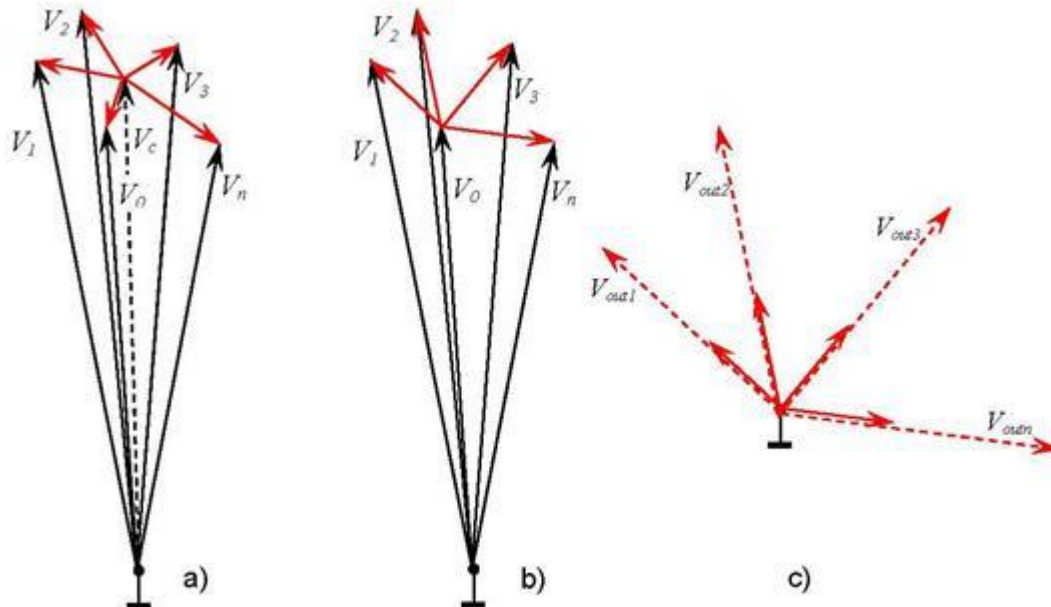
Substituting the output voltages of the first stages:

$$V'_0 - V'_i = (V_0 - V_i) \frac{R_A + R_B}{R_B} \quad (3.29)$$

Expressing $V_{out\ i}$:

$$V_{out\ i} = (V_0 - V_i) \left(\frac{R_A}{R_B} + 1 \right) \frac{R_D}{R_C} \quad (3.30)$$

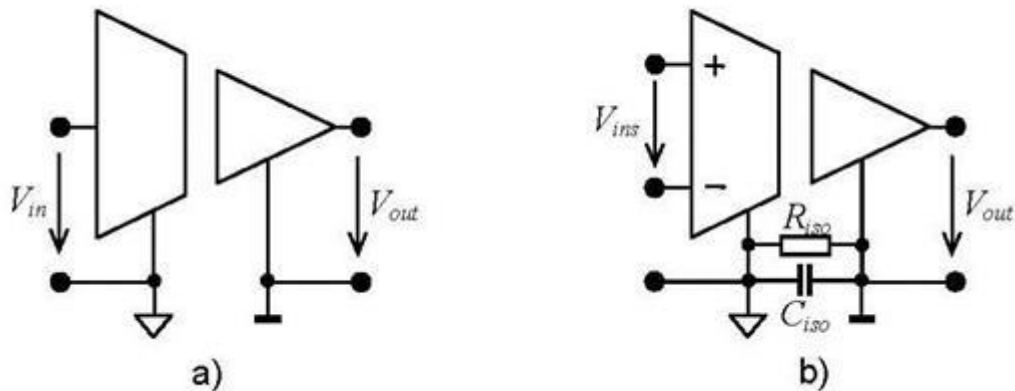
Figure 3.20. Figure 3.20. Vector diagrams of the multichannel amplifier shown in Figure 3.19. The input stages amplify the differential voltages given in red (a), the $V_0 - V_i$ differential voltages (b) and the amplified $V_{out\ i}$ voltages (c).



6. Isolation amplifiers

There is no galvanic connection between the input and output of an isolation amplifier [3.12], [3.13], [3.14]. This is advantageous both for safety and for keeping the noise level low. Isolation amplifiers (see symbol in Figure 3.21) help cancel ground loops. In addition to the usual parameters further features are the impedance between the isolated parts ($R_{iso} = 10^9 \dots 10^{14} \Omega$, $C_{iso} = 2 \dots 10 \text{ pF}$) and the isolation barrier (typical electrical breakdown is $1 \dots 4 \text{ kV}$). This is higher by orders of magnitudes than the maximum common voltage allowed for instrumentation amplifiers.

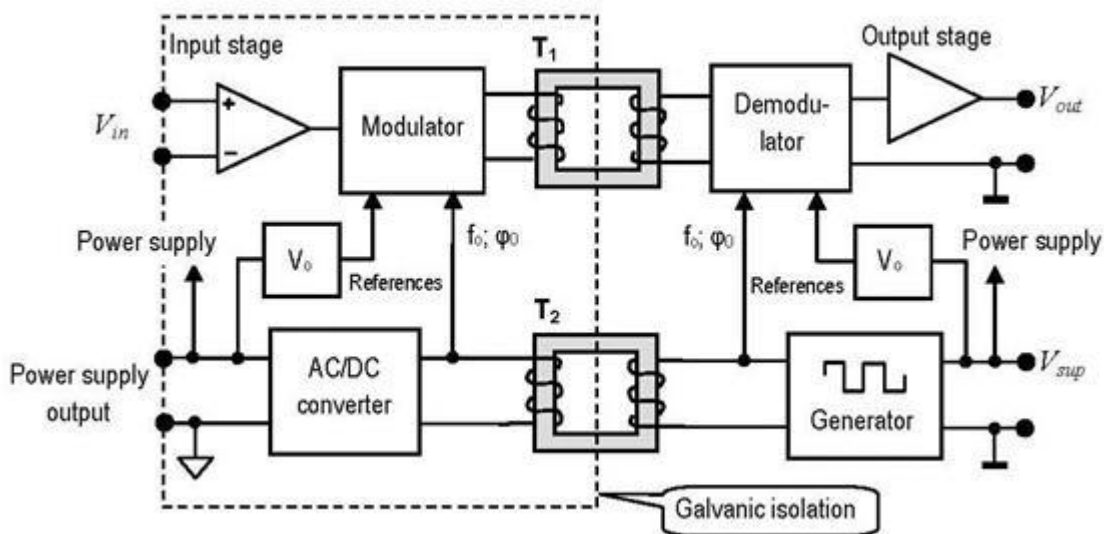
Figure 3.21. Symbols of asymmetric (a) and symmetric (b) isolation amplifiers. In (b) the isolation impedance is also drawn.



6.1. Transformer coupling

In bioamplifiers small transformers should be used for inductive coupling. This is possible if the applied frequency is relatively high ($50 \dots 400 \text{ kHz}$). A square wave signal is generated in the output stage and this is transferred to the input stage. The square wave not only conveys power to the input stage it also serves as a reference (frequency and phase). V_{in} is amplified and then modulated with the square wave and transformed through T_1 to the output stage. The demodulator uses the same square wave for phase coherent operation.

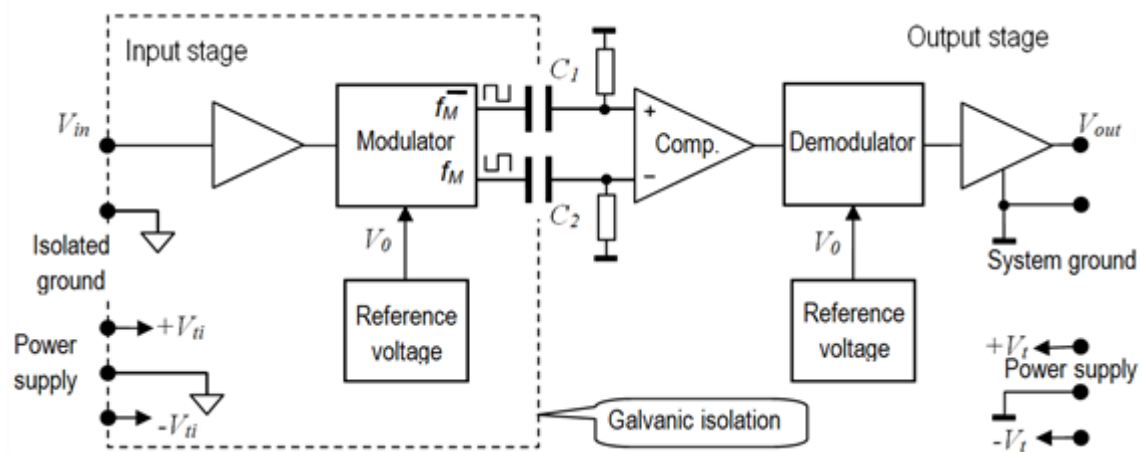
Figure 3.22. Transformer coupled isolation amplifier



6.2. Capacitive coupling

Capacitive coupled isolation amplifier can be cheaper and easier integrated than transformer coupled but the galvanically isolated input stage but the power supply of the input stage cannot be generated by signals from the output stage. The input signal after amplification is led to a voltage-frequency converter. Matched capacitors C_1 and C_2 (1 ... 3 pF, with high breakdown voltage) transmit the signal across the isolation barrier to a symmetrical input comparator. The comparator senses only the push-pull frequency modulated signal and suppresses the voltage between the two sides as it is common voltage. The demodulated signal is amplified to produce the output voltage V_{out} .

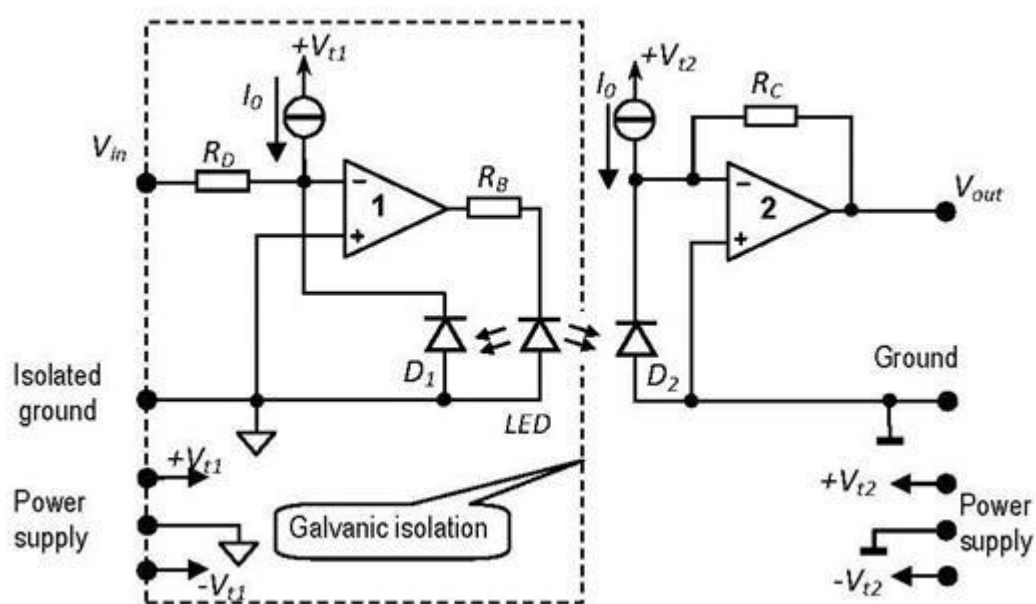
Figure 3.23. Capacitively coupled isolation amplifier



6.3. Optical coupling

If the required accuracy is moderate optical coupling is a simple and cheap solution for isolation (see Figure 3.24). For bipolar signals an offset (with I_0 current generators) is necessary on both stages as optical transmitters (D₁, D₂, and LED) operate only with a given current direction. The LED illuminates two photodiodes (for this purpose a LED packaged together with two photodiodes is available). One diode transfers the signal to the output stage the other diode is part of a feedback loop in the input stage. Application of two LEDs eliminates most of the errors of the LED and the diodes (temperature dependence, nonlinearity, ageing). As no modulation is necessary optical coupling can realize the highest bandwidth ($f_{max}=50\text{-}200$ kHz).

Figure 3.24. Simple optically isolated amplifier



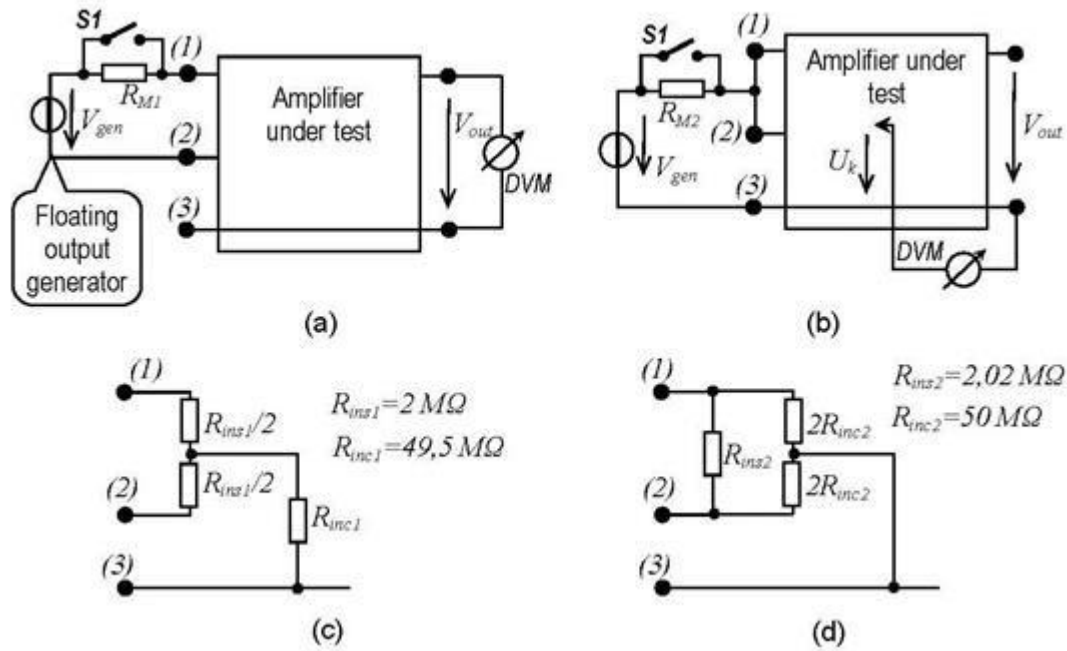
6.4. Power supply for galvanically isolated stages

Galvanically isolated input stages need power supply. It can easily be realized with transformer coupling. Other coupling modes often apply batteries or photocells. Small power consumption makes it possible to include digital signal processing in the galvanically isolated stage and using wireless (Bluetooth, wifi, etc.) communication or optical cable.

7. Problems

1. The gains of three stages in an amplifier are 20 dB, 6 dB and 40 dB. Calculate the resultant gain. Calculate the amplitude of the input signal if the effective value of output sine wave is 1.4 V.
2. The input voltages of a symmetrical amplifier are: symmetrical $V_s = 0.5$ mV, common $V_c = 2$ V. Calculate the output symmetrical voltage and the error caused by the common voltage, if the parameters of the symmetrical amplifier are: $A_{vs}=10^3$ and CMRR = 120 dB.
3. We test a symmetrical amplifier, see Figure 3.6. We connect inputs (1) and (2) and apply a 3 V amplitude 20 Hz frequency sine wave between the connected points and (3) (common voltage). The amplitude of the output voltage is $V_{out} = 30$ mV. Next we connect (1) and (3) and apply a 2 mV amplitude 20 Hz frequency sine wave between the connected points and (2) (symmetrical and common voltage). The amplitude of the output voltage is $V_{out} = 2$ V. Calculate the A_{vs} , A_{vc} and CMRR parameters. We commute inputs (1) and (2) and repeat the measurements. What can be expected?
4. We want to measure the input impedances of a symmetrical amplifier. We measure at a frequency where the impedances are real, $Z_{in} = R_{in}$. During the measurement it has to be taken into account that the input impedance of the amplifier can be higher than the input impedance of the voltmeter. This explains measurement shown in Figure 3.25.a and b. When switch S1 is open, resistor R_M and the input resistance of the amplifier divides the voltage of the generator. The input voltage of the amplifier is not measured directly it is calculated based on the output voltage that is proportional to it.
 - a. We measure according to Figure 3.25.a. When S1 is closed $V_{out} = 1$ V_{eff}. Opening S1 the output voltage drops to 0.66V_{eff}. $R_M = 1$ M Ω . Calculate R_{ins} symmetrical input resistance.
 - b. The common input resistance can be measured if the $V_c = V_{inc}$ voltage (the upper terminal of R_{inc1} in Figure 3.25.c) can be measured in the input stage, see Figure 3.25.b. When S1 is closed, we measure $V_c = 1$ V_{eff}, when S1 is open, we measure $V_c = 0.83$ V_{eff}. $R_M = 10$ M Ω . Calculate the R_{inc} common input resistance.
5. Compare the two possible equivalent circuits for the input impedances of symmetrical amplifiers. Figure 3.25.c shows the star, 3.25.d the delta model. Calculate the elements of the two models if the measured values are: $R_{ins} = 2$ M Ω , $R_{inc} = 50$ M Ω . The figure shows the result of the calculation proving that the two models give very similar values.

Figure 3.25. Measuring the input resistances of symmetrical amplifiers (a, b), and two possible equivalent circuits to model the input resistances (c, d)



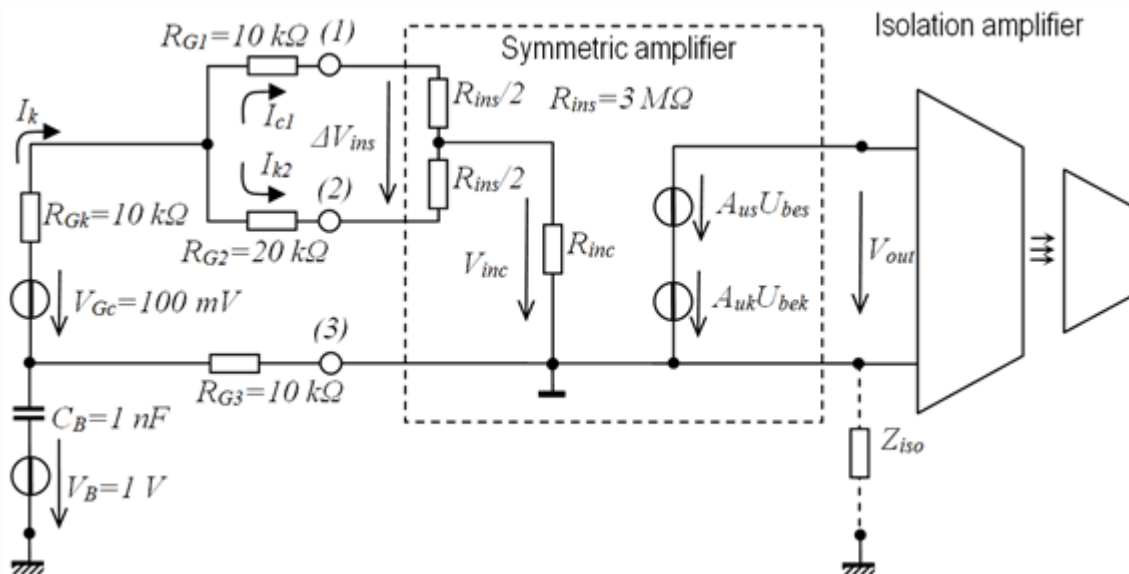
6. We analyse the effect of noise using a symmetrical amplifier connected to a patient. Figure 3.26 shows the equivalent circuit of the measurement. All impedances are supposed to be real, all $Z_G = R_G$ and $Z_{iso} = \infty$. Component values are given in the figure. Calculate the ΔV_{ins} error voltage caused by the V_{Gc} common voltage if

a. $R_{inc} = 100 \text{ M}\Omega$

b. $R_{inc} = 1 \text{ G}\Omega$

Compare the result to the symmetrical signal not specified in the figure: $V_{ins} = 0.1 \dots 1 \text{ mV}$ (e.g. ECG signal). Calculate the $\text{CMRR}_{\text{imbalance}}$.

Figure 3.26. Common voltage resulting in symmetrical error voltage



7. In Figure 3.26 the symmetrical input stage is followed by an isolation amplifier. The internal ground of the symmetrical amplifier is connected to ground through Z_{iso} composed of stray capacitances, $C_{iso} = 200 \text{ pF}$. Calculate the common voltage increase through C_{iso} in the input stage if the frequency of V_B is 50 Hz. What is the increase if the frequency of V_B is higher?

8. The input overload protection of an amplifier is according to Figure 3.17.a. The serial resistor is $R_v = 390 \text{ k}\Omega$. The forward voltage drop of the diode with low reverse current is $V_D = 0.8 \text{ V}$. The operator touches the input with a static charge equal to a $C = 150 \text{ pF}$ capacitor charged to 8 kV . Give the waveform and peak value of the current flowing through R_v . Calculate the energy dissipated on the diode and on R_v as a result of the static charge.
9. External high frequency noise signals must be prevented from getting into the amplifier. High frequency signals can saturate the amplifier; distort the signal to be measured. A low-pass filter is formed using the resistor of the overvoltage protection circuit ($R_v = 390 \text{ k}\Omega$) and a $C_p = 22 \text{ pF}$ capacitor in parallel with the protected input. Calculate the frequency above which the RC filter suppresses the high frequency noise at least by 20 dB.
10. Analyse the operation of the circuit given in Figure 3.24. Calculate the value and the direction of the current flowing through D1 photodiode when $V_{in} = 0 \text{ V}$. What is the mode of operation of D1 photodiode?

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9. Appendix

At the very beginning of telecommunication (~ 1900) the advantage of using logarithmic units was recognized. The logarithmic value of the ratio of two values of a given physical quantity is given. The logarithm to base 10 (common logarithm) is used, the notation is: $\lg(x/y)$ or $\log_{10}(x/y)$. The advantage of using logarithmic ratio:

- There are physical quantities that vary over a broad range: the ratio of analogue voltages in an amplifier can be between 1 and 10^6 , the maximum/minimum intensity of visible light is around 10^{14} . This makes illustration on a linear scale useless.
- The intensity/amplitude of signals progressing along a long line in homogeneous medium attenuates exponentially; the plotting on a logarithmic scale is expressive.
- Human visual and auditory system has a logarithmic scale.
- The gains and attenuations of stages in an amplifier give the resultant gain by multiplication. Using the logarithmic scale addition has to be used instead of multiplication. Especially for illustration (e.g. gain vs. frequency plot) addition is advantageous.

The unit used for expressing the ratio of intensities is bel [B] (named after A. G. Bell Scottish scientist and inventor).

$$a[B] = \lg \frac{P_2}{P_1}$$

In practice the unit one tenth of bel, the decibel (dB) is used:

$$a[dB] = 10 \lg \frac{P_2}{P_1}$$

The above ratio of power can be calculated based on voltage if they produce power on identical resistors:

$$P_1 = \frac{V_1^2}{R} \quad \text{and} \quad P_2 = \frac{V_2^2}{R}.$$

$$a[dB] = \lg \frac{V_2^2}{V_1^2} = 10 \lg \left(\frac{V_2}{V_1} \right)^2 = 20 \lg \frac{V_2}{V_1}$$

The above logarithmic expression of voltage ratio is used even for voltages falling on different resistors. In this case the ratio does not express the power ratio; usually we are not interested in that.

The situation is similar for the intensity and amplitude of ultrasound wave.

Intensity I is the power P over unit area A :

$$I = \frac{P}{A} \left[\frac{W}{m^2} \right]$$

The output signal of ultrasound detectors is proportional to the p sound pressure. The relation of intensity and sound pressure is:

$$I = \frac{p_{eff}^2}{Z}$$

where Z is the acoustic impedance. The attenuation of ultrasound propagating in a given substance can be expressed by the ratio of intensity and also by the ratio of sound pressure:

$$10\lg \frac{I_2}{I_1} = 10\lg \frac{p_2^2}{p_1^2} = 20\lg \frac{p_2}{p_1}$$

The attenuation or reflection coefficient may refer to the ratio of intensities or amplitudes resulting in different values expressed in dB.

The value of several physical quantities is given using logarithmic scale so that the 0 dB level is fixed. In electronic signal transmission the reference power level is 1 mW. The power level referenced to 1 mW is denoted by dBm.

$$PowerLevel [dBm] = 10\lg \frac{P}{P_0} = 10\lg \frac{P}{1\text{mW}}$$

In acoustics sound pressure level is referenced to 20 µPa which is the average human threshold of hearing. The sound pressure level expressed in dB:

$$L_p [dB] = 20\lg \frac{P}{p_0} = 20\lg \frac{P}{20\mu Pa}$$

Voltage ratios expressed in dB:

V₂/V₁	0,01	0,1	0,5	0,707	0,89	1	1,12	1,41	2	10	100
dB	-40	-20	-6	-3	-1	0	1	3	6	20	40

Chapter 4. Biosignal processing

1. Improving signal to noise ratio

Readers are supposed to be familiar with the signal processing methods used in this chapter. References [4.1] – [4.11] give detailed description about the methods in general. The aim of this chapter is to illustrate how these methods can be applied for biosignals: what is the effect of filtering on the signal (not only on the noise). In the general case only the sum of signals of different origin can be assessed. Usually we are interested in only one component of the measured signal called signal, all other components are regarded as noise. Table 4.1 gives examples of electrical biosignals.

Table 4.1. Electrical biosignals

Organ	Name of the signal	Short name	Typical frequency range	Typical amplitude range
heart	electrocardiogram	ECG	0.05 – 100 Hz	0.5 ... 2 mV
brain	electroencephalogram	EEG	0.5 – 80 Hz	10 ... 200 μ V
muscle	electromyogram	EMG	0.1 – 10 000 Hz	50 μ V ... 5 mV
eye	electrooculogram	EOG	DC – 50 Hz	10 μ V ... 2 mV
intestines	electrogastrogram	EKG	0.05 – 0,3 Hz	10 μ V ... 0,5 mV
nerve	electroneurogram	ENG	0.1 – 10 000 Hz	10 μ V ... 2 mV

Biosignals given in Table 4.1 can only be measured added up with other signals – called noise. The most common noise sources are: power line noise, electromagnetic radiation of different electronic devices, etc. When we measure ECG all other biosignals (mainly EMG) mean noise! A special case is measuring foetal ECG when mother's ECG is noise. Not only is her ECG much higher in amplitude, but the shape of the two signals is quite similar making separation difficult.

Figure 4.1 shows a 5-s segment of a 100-s ECG record taken with stainless steel electrodes from the left- and right hand of the tested person. Figure 4.2 shows the frequency spectrum of the 5-s segment after removing the DC component. There is a substantial 50 Hz power line noise. This makes the evaluation difficult. Diagnostic signal processing requires the increase of signal-to-noise ratio with the smallest possible distortion of ECG signal.

Figures in this chapter were made using Matlab R2007b (copyright 1984-2007, The Mathworks Inc.). We suggest using Octave (<http://www.gnu.org/software/octave/>), a freely available program quite similar to Matlab. The recordings shown in this chapter were made with a home health monitoring device HHM [4.12], [4.13] and a passive marker based movement analyser PAM [4.14] developed at the Department of Measurement and Information Systems Budapest University of Technology and Economics. The complete records and a great number of other records are available www.mit.bme.hu/~jobbagy/mon web page. The reader is suggested using these records to practice the application of signal processing algorithms shown in this chapter.

Figure 4.1. ECG record with substantial power line noise, taken with limb electrodes on wrists

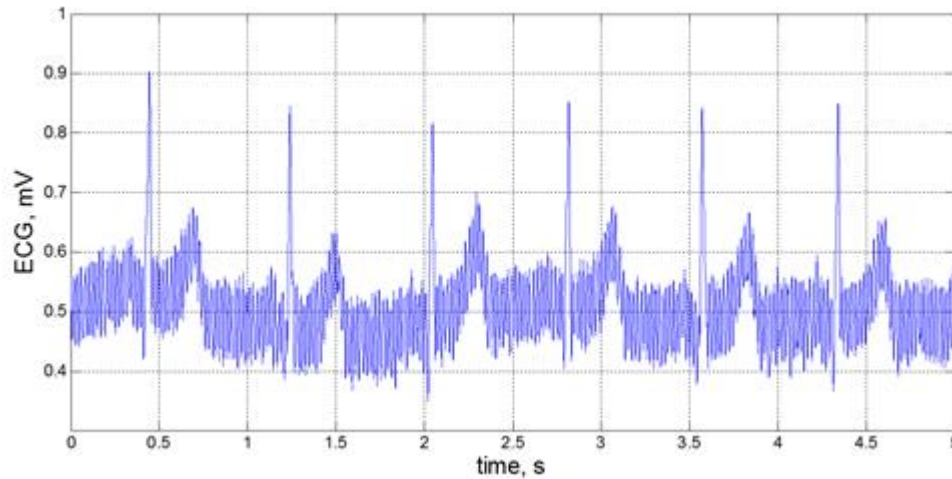
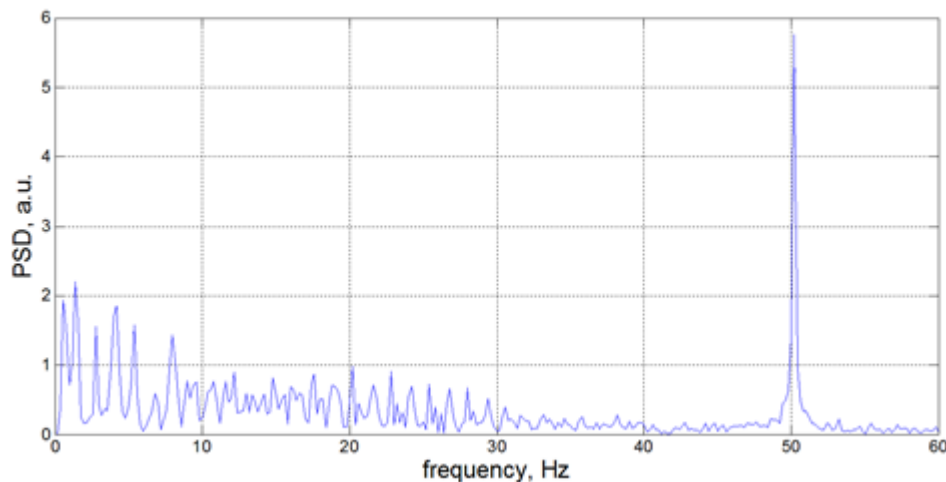


Figure 4.2. Frequency spectrum of ECG record shown in Figure 4.1 (DC removed before computation)



Low-pass or band-stop filters can be used to suppress power line noise. The frequency range of power line noise and of biosignals to be measured overlap. The frequency spectrum of resting ECG is 0.05 – 100 Hz. Power line noise (in Europe 50 Hz) is within this range. As a consequence, suppressing power line noise by filtering in the frequency domain affects also the ECG signal. Only the sum of ECG signal and noise can be measured, the noise free signal is not available. Thus, the distortion of ECG as a result of filtering (to suppress power line noise) is difficult to be evaluated. We analyse the phenomenon by generating ECG signal and adding to it noise with known parameters. In this case the noise free signal is available; the filtered signal can be compared to it. The distortion effect of filtering in the frequency domain can be evaluated quantitatively. Low-pass filtering in the frequency domain (second order Butterworth, with 30 Hz corner frequency) is applied to the ECG signal given in Figure 4.1. Figure 4.3 shows the resulting signal.

Figure 4.3. The ECG signal given in Figure 4.1 (blue) and its low-pass filtered version (second order with corner frequency 30 Hz, Butterworth) (red)

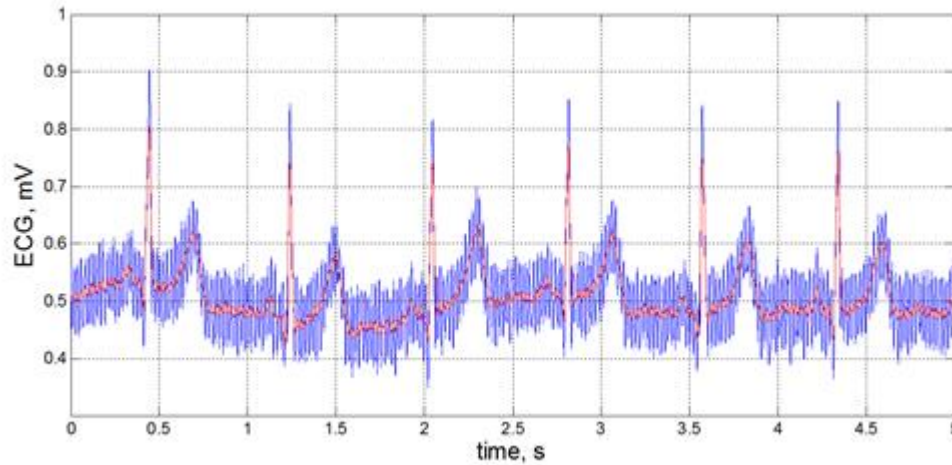


Figure 4.4. The frequency spectrum of signals given in Figure 4.3: original ECG (blue) and filtered (red)

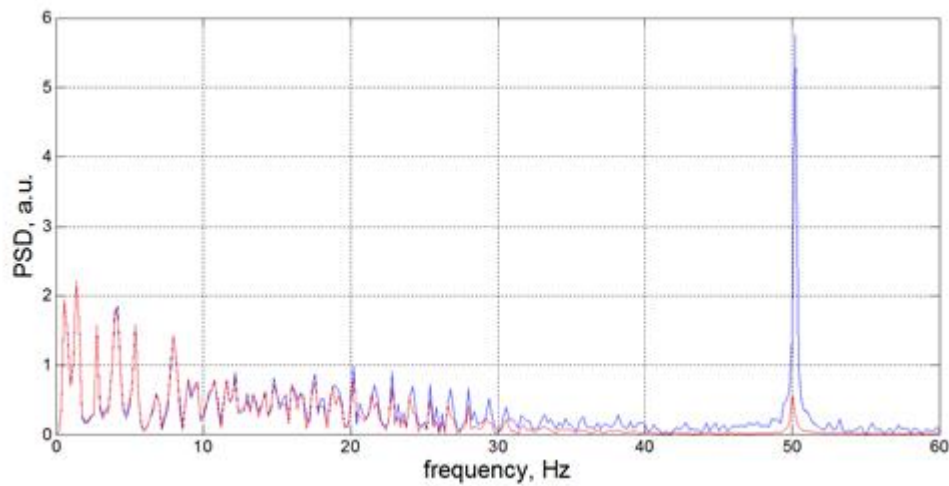
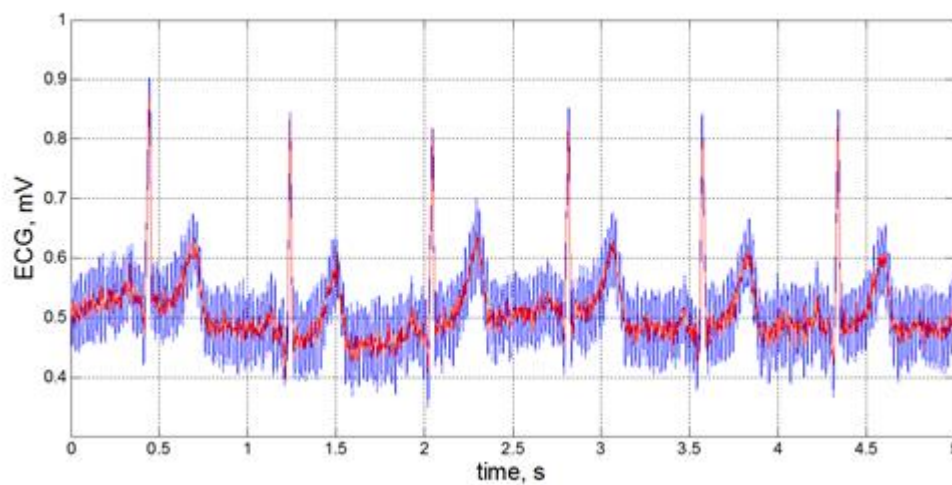


Figure 4.5. The ECG signal given in Figure 4.1 (blue) and its band-stop filtered version (second order with centre frequency 50 Hz, Butterworth) (red)



Power line noise decreased substantially. At the same time QRS amplitudes also decreased! The frequency spectrum (Figure 4.4) illustrates that components of ECG above 15 Hz (half of the corner frequency) are attenuated.

Figure 4.5 shows the effect of a 50 Hz band-stop filter (second order Butterworth). The QRS amplitudes are attenuated with this filtering, too. The frequency spectrum shows (Figure 4.6) that band-stop filtering eliminated 50 Hz noise. However, the noise in the time function seems to be higher than after low-pass filtering (compare Figures 4.3 and 4.5). The reason is that band-stop filtering does not attenuate the harmonics of 50

Figure 4.6. Frequency spectrum of time functions in Figure 4.5

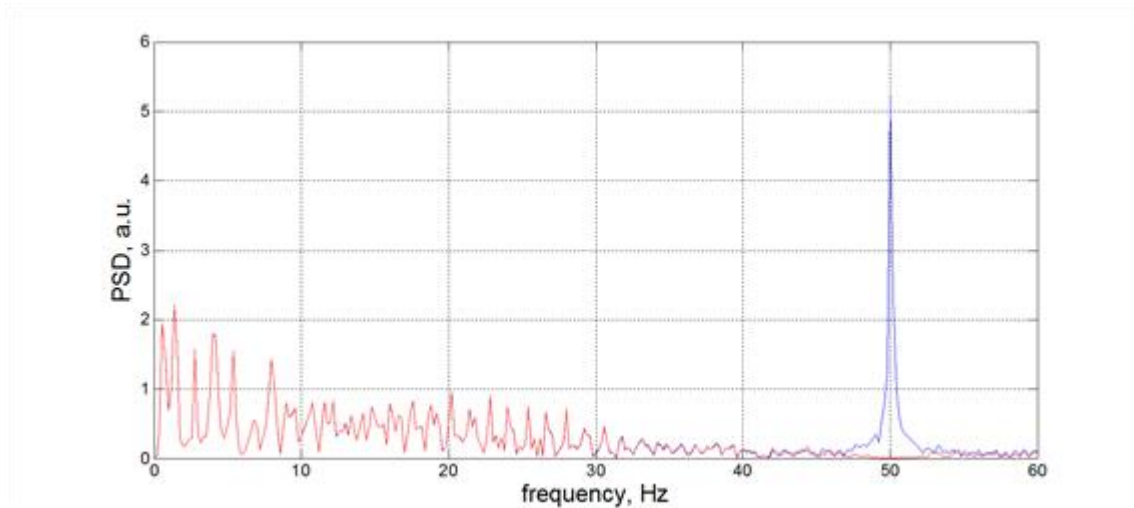
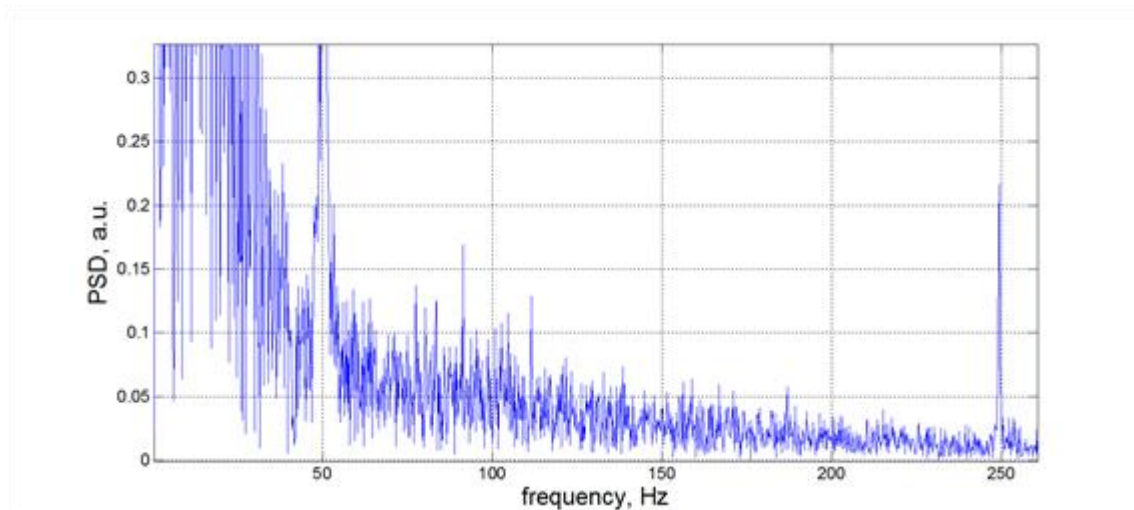


Figure 4.7 shows the frequency spectrum of the signal before filtering in the 0 – 300 Hz band.

Figure 4.7. Figure 4.7. The frequency spectrum (DC – 300 Hz) of the ECG signal given in Figure 4.1.



Based on Figure 4.7 the noise in the ECG time function is mainly around 250 Hz. Figure 4.8 shows the frequency spectrum of the total 100-s ECG record in the 0 – 300 Hz band. The third harmonic (150 Hz) is present in the spectrum computed for the whole record contrary to the spectrum computed for the first 5 s only, where the 150 Hz component is negligible. Most probably the stray capacitances were not stable between the body of the tested person and the hot wire and ground of the power line. As a result, the shape of the power line noise on the body surface and so the harmonics in the frequency spectrum were varying during the measurement.

Figure 4.8. Frequency spectrum (DC – 300 Hz) of the 100-s ECG signal of which Figure 4.1 shows the first 5-s

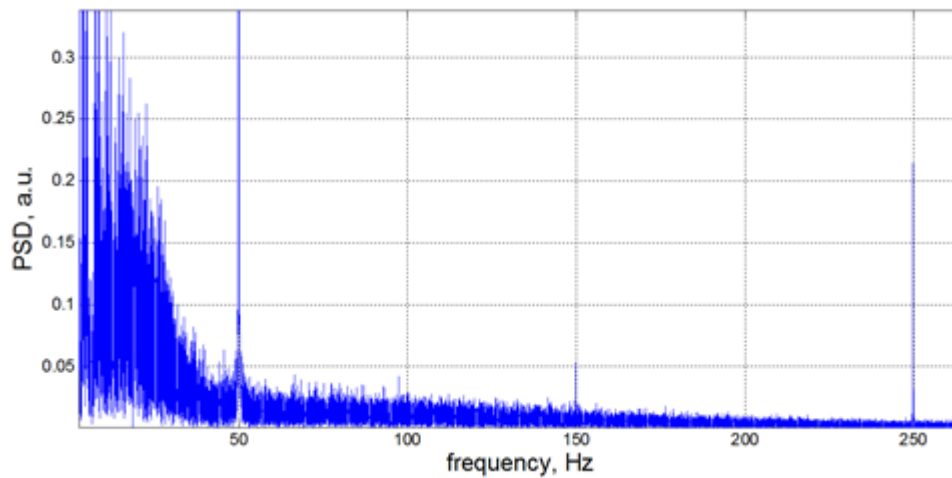
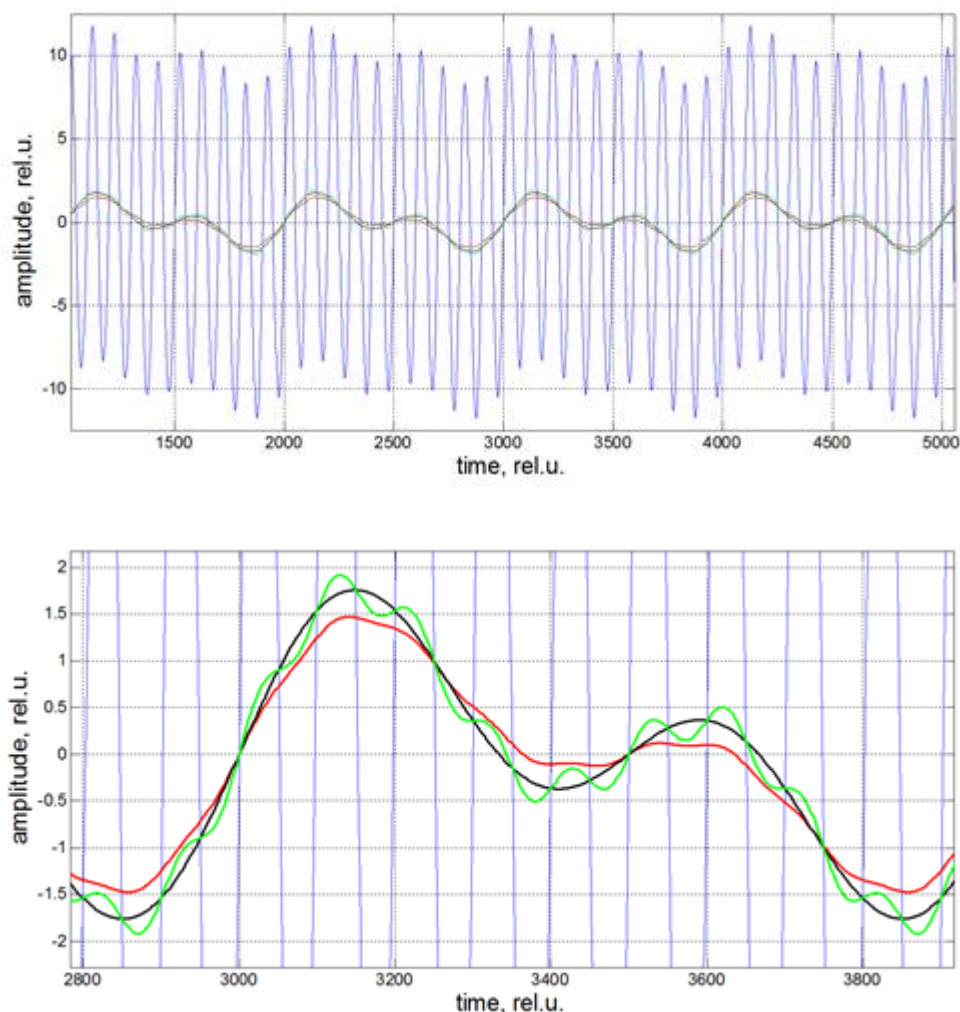


Figure 4.9. a.) Frequency domain filtering. Signal plus noise (blue), following low-pass filtering (red). The noise-free signal (black). The sum of the noise-free signal and the noise divided by 20 (green). b.) One period enlarged from subfigure a.) Illustrating the effect of frequency domain filtering, using synthesized input signal

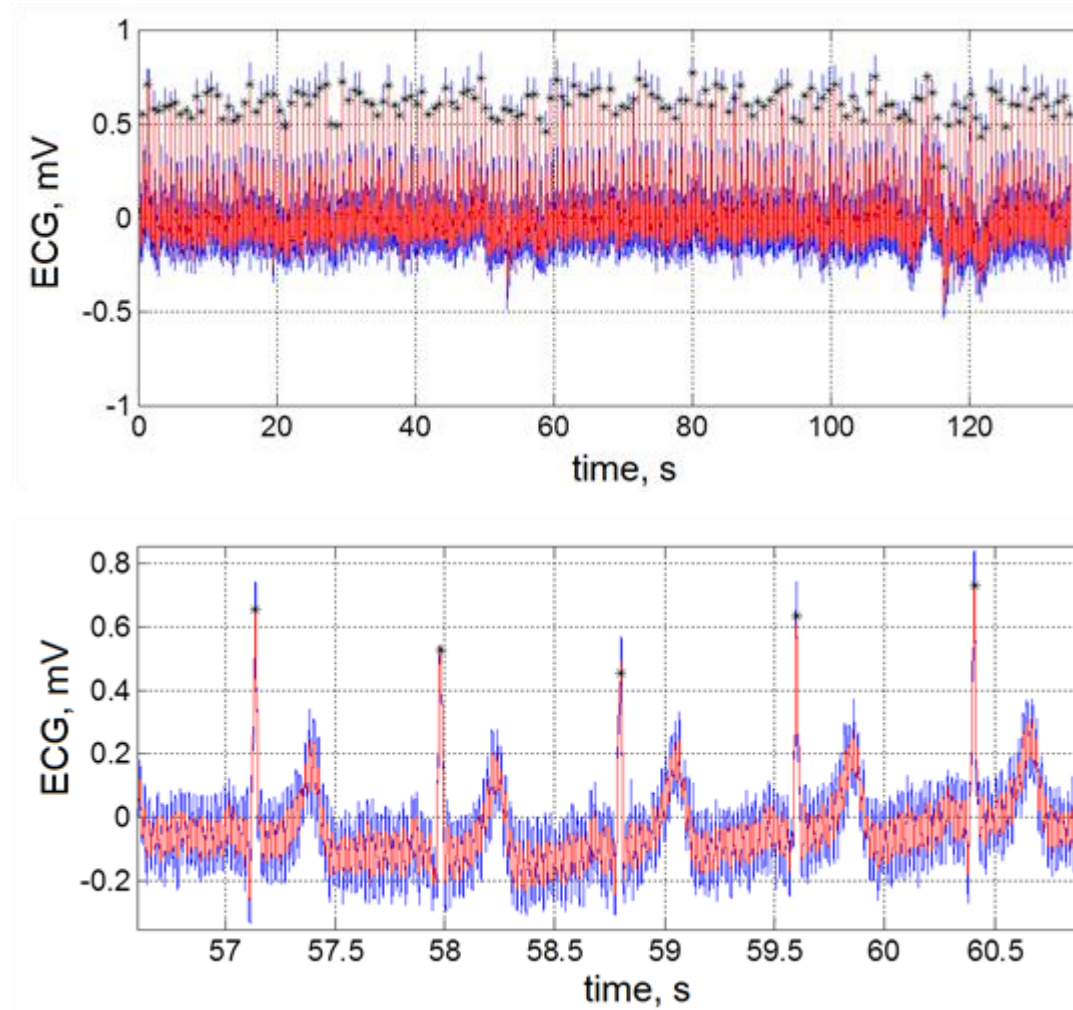


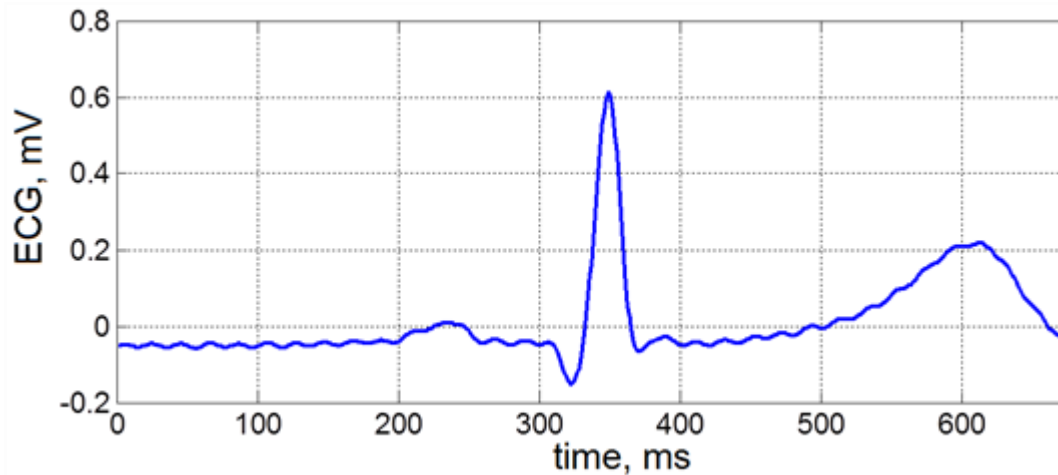
Let's analyse the effect of filtering using artificial signals. When we generate the input signal then the ideal noise-free signal is known (contrary to the noisy ECG signal recorded from a patient.) The first ideal signal is the sum of two sine waves with the same amplitude (A_0) and frequencies f_0 and $2 \times f_0$ see eq.4.1. The signal is drawn in black in Figure 4.9.a. The noise added has amplitude of $10 \times A_0$ and frequency $10 \times f_0$, see eq. 4.2.

$$y_{id}(t) = A_0 \sin(2\pi f_0 t) + A_0 \sin(2\pi 2f_0 t) \quad (4.1)$$

$$y_{noise}(t) = 10A_0 \sin(2\pi 10f_0 t) \quad (4.2)$$

Figure 4.10. Generating the characteristic ECG cycle by averaging





The sum of the ideal signal and the noise is drawn in blue. The blue signal after low-pass filtering (second order Butterworth, corner frequency $2.5 \times f_0$) is drawn in red. Multiplying the noise signal by 0.05 and adding it to the ideal signal we get the green signal. Figure 4.9.b shows one cycle of the ideal signal. Figure 4.9.a shows that low-pass filtering attenuates the noise substantially. Figure 4.9.b shows that low-pass filtering distorts the ideal signal, too! Attenuates its amplitude and changes the shape. This latter effect is because the gain of the low-pass filter is different at frequencies f_0 and $2f_0$. If we had the possibility to attenuate noise *independently of the ideal signal* then the ideal signal would not be distorted.

The ideal noise-free biological signal is not available. The measured signal is the sum of the ideal signal and the noise. Evaluating the characteristics of the possible frequency domain filtering methods we have to select which fits best to a given application. In other words, which is optimal for increasing the signal-to-noise ratio. The general purpose methods are given in [4.1] to [4.5]. References [4.6] – [4.11] detail biosignal processing methods.

The signal-to-noise ratio can be increased also by averaging. Averaging is an effective tool if the ideal signal is periodic, uncorrelated with noise and an appropriate trigger signal (that belongs to a given phase in each cycle) is available. ECG signal is quasiperiodic; the trigger signal has to be generated from the noisy signal. The cycles of the ECG signal cannot be aligned by linear transformation of time. When the duration of a heart cycle changes its segments change differently. As a rule segments with high steepness (mainly the QRS complex) lengthen or shorten less than flat segments (e.g. PQ, TP). The proper averaging of ECG signals aligns the cycles at the QRS peaks so that they are in the middle. The time between the QRS peak and the endmost points of the cycles is half of the time we would get if one cycle would last from R peak to R peak. As a result the effect of non-uniform lengthening and shortening will be smaller. Averaging means a low-pass filtering effect because of the non-uniform lengthening and shortening. In top subfigure of Figure 4.10 a 135-s ECG is given recorded in Einthoven I. lead. The original record is in blue, the red curve is after second order Butterworth low-pass filtering (corner frequency 30 Hz). Black stars mark the QRS peaks (Pan – Tompkins algorithm was used). In the middle subfigure five cycles are magnified. As a result of low-pass filtering the QRS amplitudes are attenuated while power line noise remained substantial. The bottom subfigure shows the average (computed as given above) of the 162 cycles. Notice the improved signal-to-noise ratio.

Transformation of a given record to the frequency domain is most often done with FFT (Fast Fourier Transform). The resulting spectrum gives the frequency components present over the complete recording time. It does not give information about the changes of the components in time.

A major dilemma in biosignal processing is to select the length of recording time or time window to be processed by FFT. High frequency resolution (small Δf) requires long recording time in turn the frequency spectrum remains constant only for a short time. Possible solution is the time-frequency analysis where the signal is evaluated at the same time in both frequency and time domain. This fits to the time varying frequency spectrum. A typical time-frequency analysis is the wavelet transform [4.15].

Even in case of unfavourable signal-to-noise ratio signal components can be easily detected if their shape is known. Correlation with the known pattern (sliding it through the recording) will result in maximum values when the component with the known shape overlaps with the pattern. The original (noisy) signal in top subfigure of Figure 4.10 was analysed by correlating it with the pattern generated by averaging the cycles

(bottom subfigure of Figure 4.10). Figure 4.11 shows the original signal (blue) and the result of correlation (red). Because of distortion caused by power line noise the maximum of the correlation is present 4 ms earlier than the QRS peak (Figure 4.12) or 2 ms later (Figure 4.13).

Figure 4.11. QRS detection by pattern matching. The record shown in Figure 4.10 (blue) and its correlation (red) with the average heart cycle.

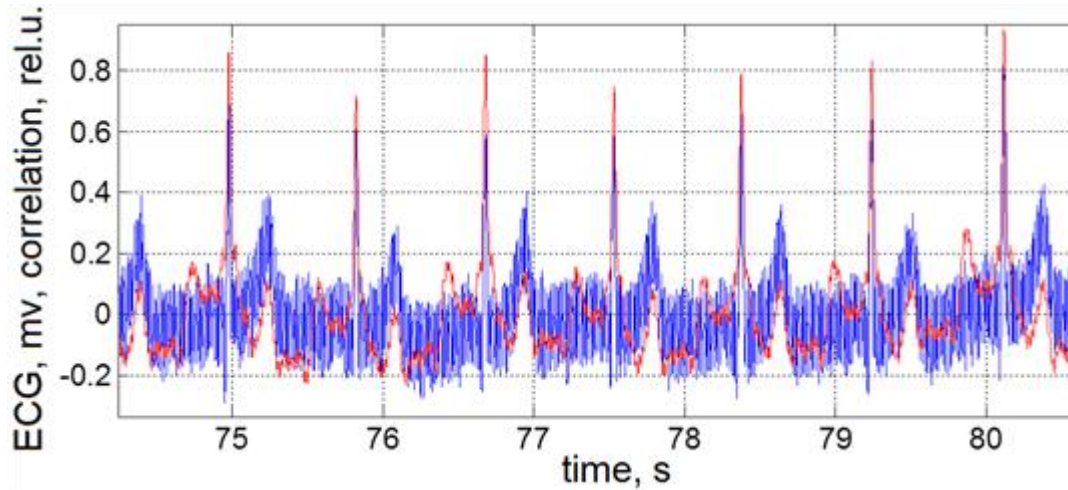


Figure 4.12. The second QRS in Figure 4.11.enlarged.

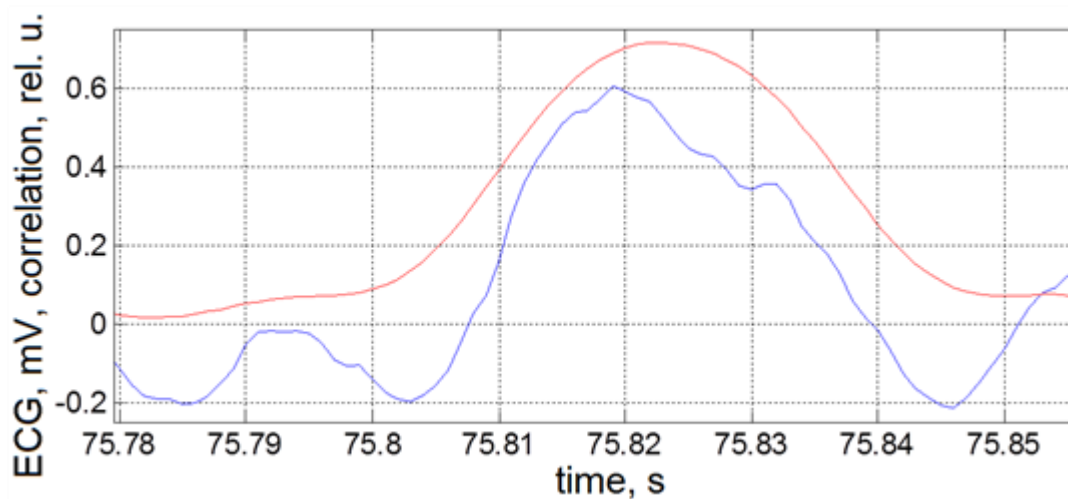
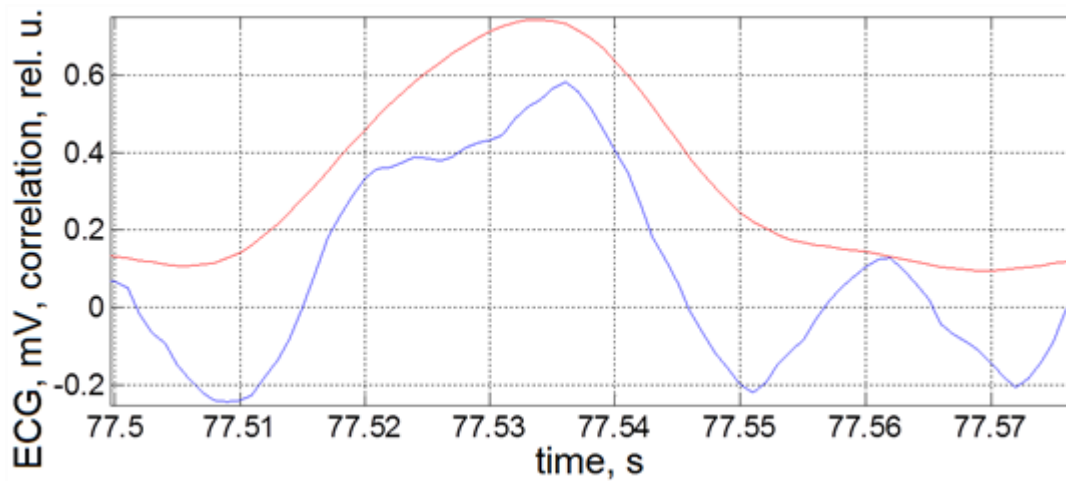
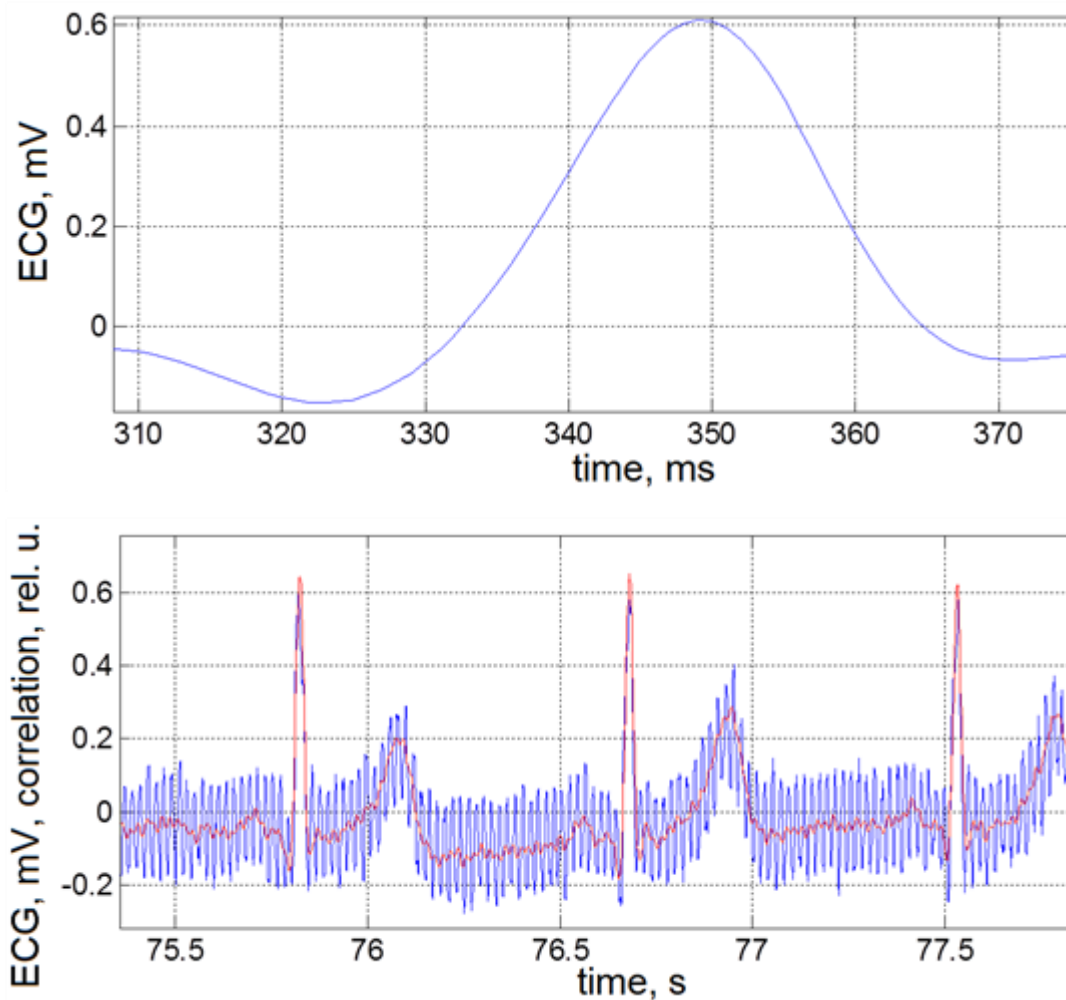


Figure 4.13. The fourth QRS of Figure 4.11 enlarged



Morphological filtering [4.30] is also basically pattern matching. First the pattern has to be composed. Its shape and length must fit to the signal and the noise to be suppressed. The correlation of the signal with the pattern (it can be realized by the `xcorr` function of Matlab) gives the filtered signal. Let the pattern be averaged QRS segment, see upper subfigure of Figure 4.14. The lower subfigure shows the original (blue) and the filtered (red, correlation with the average QRS pattern) signal along three heart cycles. The averaged QRS pattern and the power line noise are uncorrelated, the noise is suppressed substantially.

Figure 4.14. Improving signal-to-noise ratio by pattern matching



2. Evaluation of biosignals

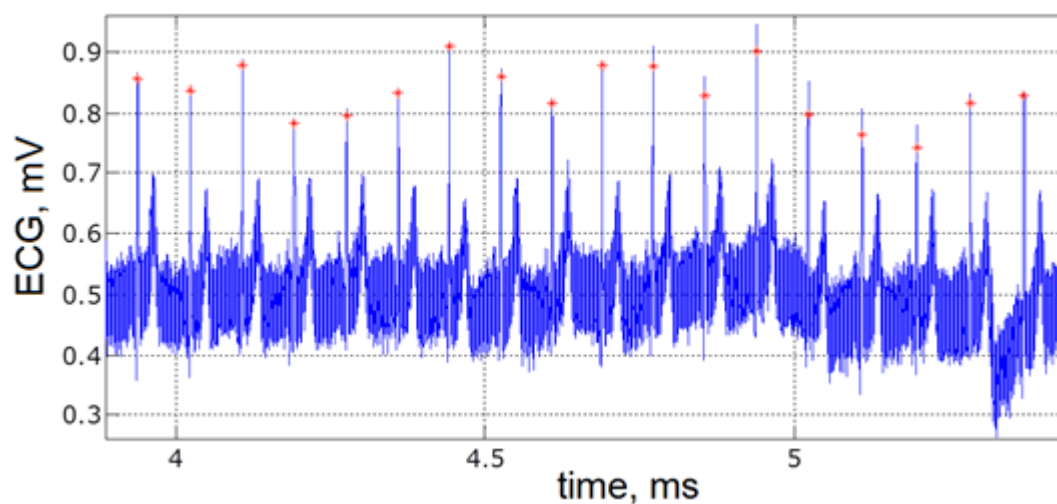
2.1. ECG signal processing

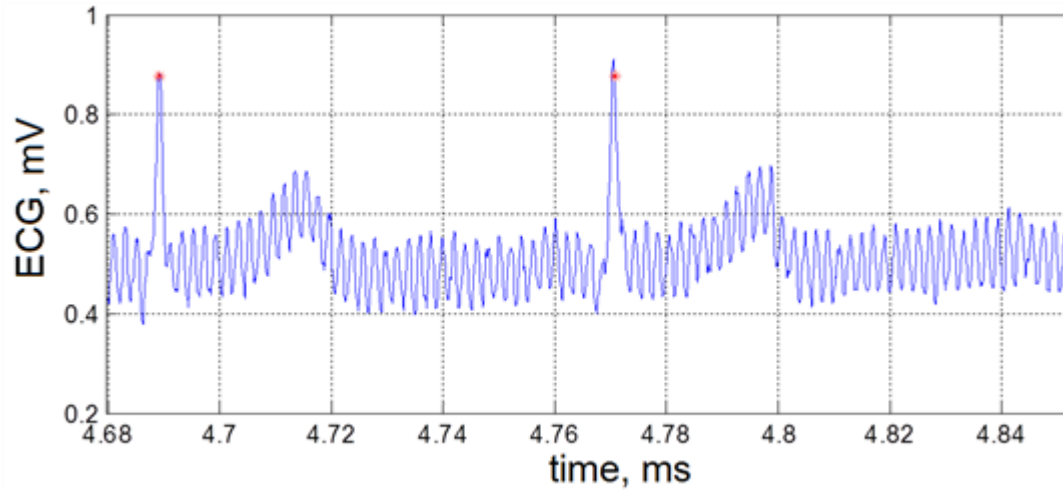
The ECG signal available on the body surface has an unfavourable signal-to-noise ratio. On the body surface the electrical activity of the heart produces around 1 mV while the power line noise around 1V amplitude. ECG amplifiers are symmetrical ones (see chapter 3.4) improving the signal-to-noise ratio substantially, their typical output signal is like Figure 4.1. The signal-to-noise ratio can be further increased by methods given in chapter 4.1.

In this chapter we will deal with the evaluation of ECG time functions recorded in a single lead (see chapter 6). Evaluation can be more effective (e.g. QRS detection) if several leads are used in parallel. Most of the recordings analysed were taken by the Home Health Monitoring (HHMD) device [4.12], [4.13] developed at the Department of Measurement and Information Systems Budapest University of Technology and Economics. HHMD records Einthoven I. bipolar lead, the electrodes are in contact with the left- and right palm. The output of the body surface potential driving amplifier is also connected to the right palm. ECG recordings analysed in this chapter were taken from subjects who had a $0 \dots 180^\circ$ degree angle between the electrical axis of their heart and the Einthoven I. vector lead (horizontal). As a result, P, R and T waves are positive. The first step in ECG signal processing is QRS detection. In the majority of cases this is a relatively simple task. Knowing the QRS positions (in time) helps the allocation of further segments (P and T wave, ST segment). QRS complex is related to ventricular depolarization; its steepness and amplitude are relatively high.

The usually poor signal-to-noise ratio makes ECG analysis difficult. The main sources of noise are: power line noise through stray capacitances (in Europe 50 Hz and its harmonics), RF noise, movement of electrodes on the skin, motion of the tested person (causing EMG signal), breathing, change of the skin/electrode interface. The latter two cause low frequency change called baseline drift. The Pan-Tompkins algorithm [4.27] is widely used for QRS detection. Figure 4.15 shows, that the Pan-Tompkins algorithm locates a point close to the R peak. The exact position of R peak requires a further maximum search in the vicinity (a few ms) of the location advised by the Pan-Tompkins algorithm.

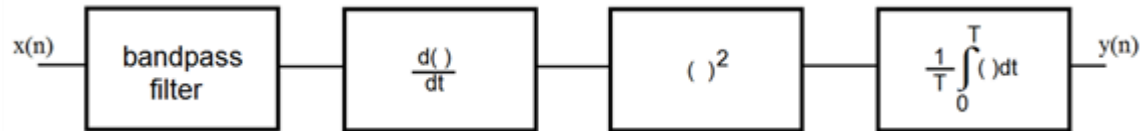
Figure 4.15. The result of QRS detection using the Pan-Tompkins algorithm. All the 19 QRS complex of the upper curve were detected but not necessarily the R peak was marked (bottom).





The functional block diagram of the improved Pan-Tompkins algorithm [4.16] is given in Figure 4.16. The steps of the algorithm are: band-pass filtering, derivation, rms calculation, integration with moving window, thresholding. Band-pass filtering (usually between 6 ... 16 Hz) is based on the fact that segments of an ECG cycle have different frequency spectrum. The maximum of QRS is between 6 ... 16 Hz; the one of P and T waves is between 1 ... 3 Hz.

Figure 4.16. Steps of the Pan – Tompkins QRS detector



The QRS detection performance can be characterized by two parameters:

1. the ratio of QRS complexes detected to all QRS complexes (selectivity),
2. the ratio of all QRS complexes to all complexes qualified as QRS (positive predictivity).

The actual signal-to-noise ratio, the activity of the tested person (at rest, stressed, healthy, different heart failures) and the stability of the heart rate influences the ratio of detected over all QRS complexes (sensitivity, S). It is more difficult to characterize the rate of erroneously detected (i.e. a segment is not a QRS but the detector qualified being so) QRS complexes. The classic definitions are: specificity = $TN / (TN + FP)$, where TN means true negative, and FP means false positive qualification. Further possible qualifications are: TP (true positive) and FN (false negative). These qualifications are unequivocal when patients are diagnosed having a certain disease based on medical check-up. True positive (TP) means the check-up indicated the illness and the patient really suffers from it. True negative (TN) means the check-up showed the patient did not have that illness and it was true. False positive (FP) means the check-up indicated the illness but the patient did not have it. False negative (FN) means the check-up showed the patient did not have the illness but the patient did have it. In case of QRS detection positive predictivity is used instead of specificity because the definition of TN along a time function is not easy. It could be interpreted so that within a heart cycle TN is incremented by one for the P and also for the T wave when they were not qualified as QRS by the detector. Positive predictivity (P^+) takes into account how many segments (e.g. P or T waves) were erroneously qualified as QRS. Eq. 4.3 is the definition of sensitivity, eq. 4.4 and 4.5 of positive predictivity [4.29].

$$S = \frac{TP}{TP + FN} \quad (4.3)$$

where TP (true positive) is the number of detected, FN (false negative) is the number of not detected QRS complexes.

$$P^+ = \frac{TN}{TN + FP} \quad (4.4)$$

where TN (true negative) is the number of correctly qualified 'not QRS' segments, FP (false positive) is the number of 'not QRS' segments, erroneously qualified as QRS. The sum of TP and FN is equal to the number of heart cycles in the record. It is not easy to decide which segments within a heart cycle should be analysed if the detector qualified them correctly or erroneously. Instead of eq. 4.4 the definition given by eq. 4.5 is used.

$$P^+ = \frac{TP}{TP + FP} \quad (4.5)$$

Increasing the selectivity of a QRS detector has the risk of decreasing the positive predictivity and vice versa. The location of other segments of a heart cycle (P and T waves, ST segment, and Q point) is easier if the position of QRS (which can usually be determined easier) is known. Apart from the third degree AV block, P wave and Q point precedes QRS, while ST segment and T wave follows it. Normal operation of the heart keeps the length of segments within given limits. For example PR should be between 120 ... 200 ms, QRS should be shorter than 120 ms. Taking into account the normal tPQ and tQRS ranges and the nearly symmetrical shape of QRS and P waves the peak of P wave should precede R peak by 130 ... 210 ms. Further details of ECG are given in chapter 6.

2.2. Evaluation of the photoplethysmographic (PPG) signal

Plethysmography measures the volume change of an organ or of the whole body. Photoplethysmography is when light is used for the measurement. An LED gives the – mostly in infrared – incident light and a photodiode senses the output light (that passed over the tested organ) intensity. The sensed light does not contain (electrical) power line noise, neither contains the PPG signal. Figure 4.17 shows the measurement on a fingertip. The figure shows the reflexive photoplethysmograph. The detector (photodiode) measures the reflected (mainly from bones) signal. The more blood is in the vessels of the fingertip the more it attenuates the light emitted by the LED. Figure 4.18 shows PPG signal recorded at the fingertip. (The output current of the photodiode was converted to voltage by an inverting amplifier.) The minimum value of the PPG signal belongs to end diastole; at this point the pulse wave – started by the systole – arrives to the fingertip. Measuring the PPG signal on different frequencies blood oxygen saturation can be determined (see chapter 2.2.5).

Figure 4.17. Reflexive photoplethysmography applied at the fingertip

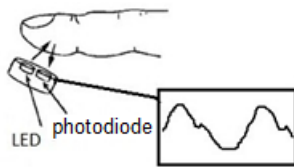
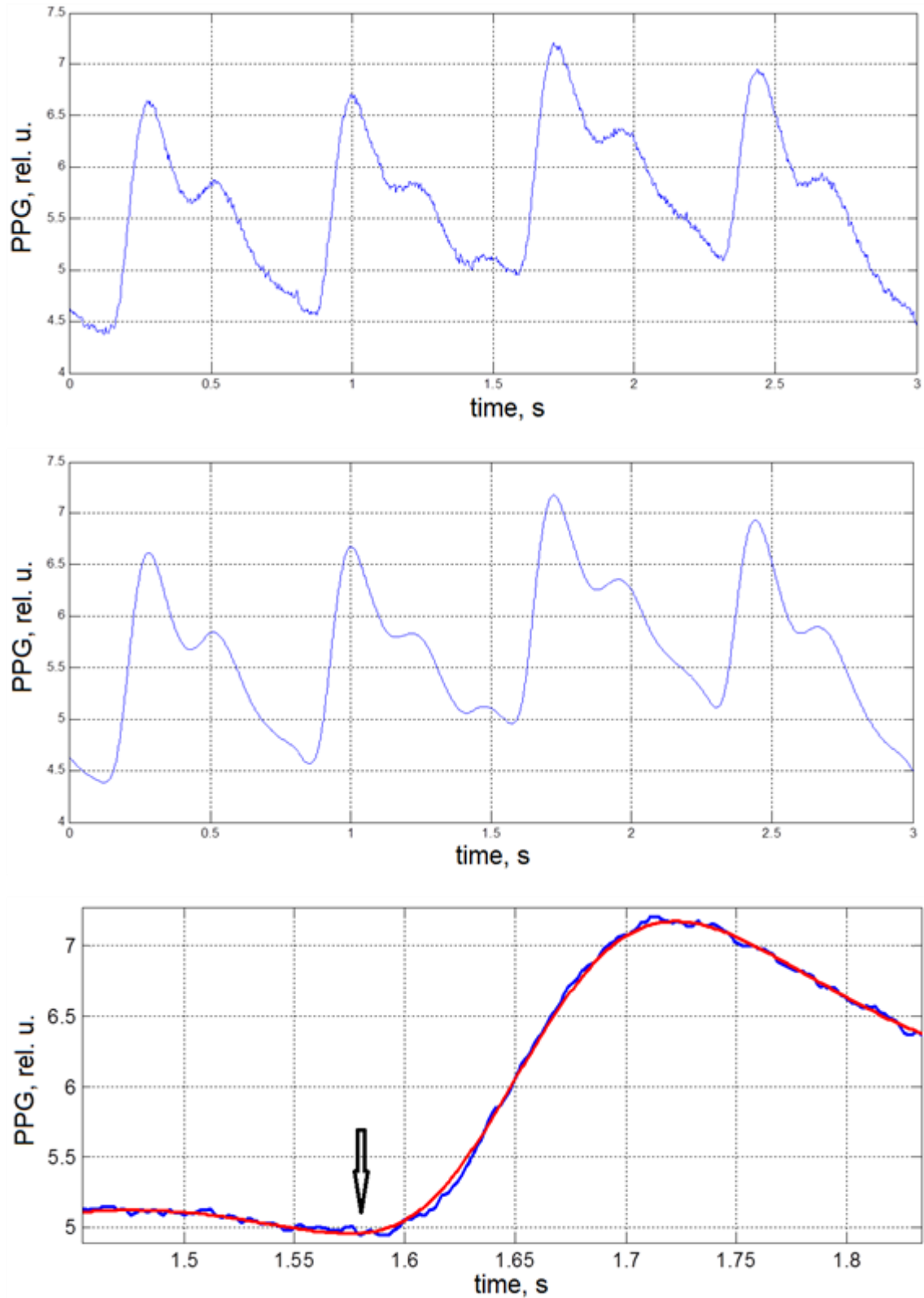


Figure 4.18 shows that following second order Butterworth low-pass filtering (corner frequency 5 Hz) the local minimum values of the PPG signal can be determined (see arrow). The local minimum is when the pulse wave resulting from ventricular systole reaches the fingertip.

Figure 4.18. PPG signal at the fingertip (top), signal low-pass filtered with a second order Butterworth filter with 5 Hz corner frequency (middle), one cycle enlarged (bottom) where an arrow marks the arrival of the pulse wave to the fingertip



When ECG and PPG are recorded in parallel the pulse wave velocity can be calculated. The R peak in ECG marks the beginning of the contraction of the left ventricle. During the first part of the contraction the pressure in the left ventricle is lower than in the aorta, thus the volume of the ventricle does not change (isovolumetric part). The pressure in the ventricle is bigger than in the atrium so the mitral (atrioventricular) valve is closed at the beginning of contraction. The increasing ventricular pressure reaches the pressure in the aorta in about 50 ms, when the aortic valve opens and the pulse wave starts. The S wave of the ECG is close to the moment when the aortic valve opens. In Figure 4.18 an arrow marks the PPG signal when the pulse wave arrives to the

fingertip. Following the arrival blood diffuses in the vessels of the fingertip decreasing the output intensity of PPG signal. The time interval from the starting and arrival of the pulse wave is called ΔT_{EP} to imply that it can be measured using the recorded ECG and PPG signals. Measuring the distance from the heart to the fingertip (d , 80 ... 120 cm), the pulse wave velocity is $v = d/\Delta T_{EP}$.

2.3. Evaluating very low frequency components

Heart rate variability (HRV) can be easily measured. It characterizes the neurovegetative activity and autonomous operation of the heart. It can be used to characterize the actual state of diabetes patients, or the stress level. Decrease in HRV prognoses certain heart failures (myocardial infarction, angina pectoris, etc.) [4.17]. From signal taken non-invasively, without the cooperation of the patient the length of heart cycles can be determined. HRV is calculated based on the lengths of heart cycles. Most often the ECG is used; the length of a heart cycle is calculated as the distance between two consecutive R peaks (t_{RR}).

HRV is characterized by its energy in basically three frequency ranges [4.18], [4.19], [4.20]. The high frequency range (HF, 0.15 – 0.4 Hz) is dominated by the parasympathetic effect. Modulation caused by breathing is also in this range. Heart rate increases during inspiration, it decreases during expiration. The low frequency (LF, 0.07 – 0.15 Hz) belongs mainly to sympathetic effects. However, parasympathetic activity under certain conditions might also affect this range. The very low frequency (VLF, 0.01 – 0.07 Hz) range is dominated by the thermoregulation. Not fully clarified is the ultra-low frequency range (ULF, 0.001 – 0.01 Hz) of HRV.

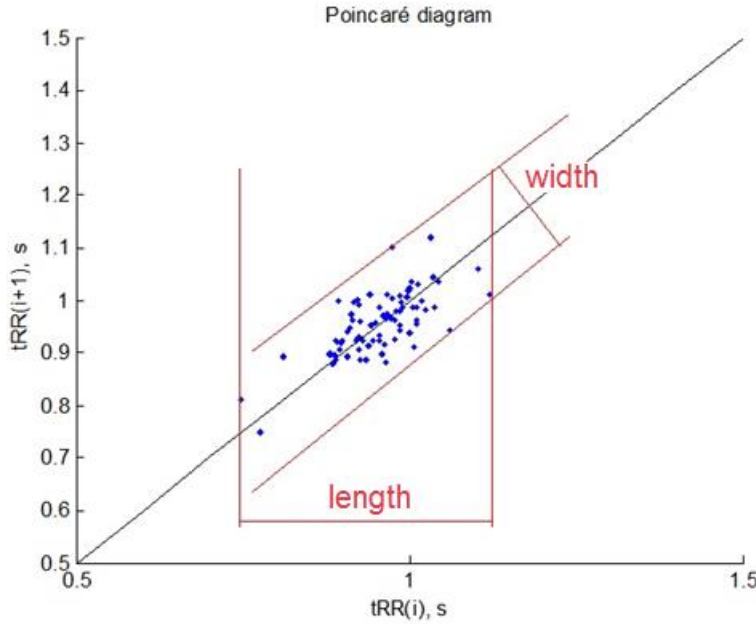
Analysis of the VLF range needs 2 mHz or better resolution. This requires at least 500-s recording. (To analyse ULF range, an order of magnitude longer!) During such a long time the biological effect to be observed and characterized does not remain constant. Stationarity of the signal is not guaranteed, not even the weak stationarity. Consequently, application of FFT to evaluate HRV is not an optimal selection. In general we have to analyse stationarity before trying to characterize slow changes of biological signals.

Analysis of HRV in the time domain means characterizing the changes in t_{RRi} values. The most frequently used parameters are:

- MSD, ms, (Mean Successive Differences of heart rate),
- SDNN, ms, (Standard Deviation of Normal-to-Normal intervals),
- SDANN, ms, (Standard Deviation of the Averages of NN intervals, typically calculated for 5 minutes), SDANN indicates changes with time period longer than the time window used; changes with shorter time period are suppressed,
- RMSSD, ms, (square Root of the Mean of the Sum of the Squares of Differences between adjacent NN intervals),
- SD or SDDSD, ms, (Standard Deviation of Differences between adjacent NN intervals),
- NN50, -, (the number of pairs of successive NNs that differ by more than 50 ms),
- pNN50, %, (percent of difference between adjacent NN intervals that are greater than 50 ms).

Poincaré diagram [4.21] characterizes HRV well. This diagram is a plot of $t_{RR(i+1)}$ values versus $t_{RR(i)}$ values. Figure 4.19 shows a Poincaré diagram generated on the basis of ECG taken from a young healthy male at rest. The width of the point set characterizes short-term variability; its length characterizes total variability. Parameters of the Poincaré diagram cannot be directly referred to parameters in the frequency domain, but under certain circumstances they have similar indications. The actual stress level can be characterized by the width of the point set or by the standard deviation of the distances of points from the 45° line (transversal standard deviation). Smaller value indicates higher stress level.

Figure 4.19. t_{RR} values of a 75-s ECG plotted on a Poincaré diagram



2.4. Evaluating the regularity of quasiperiodic signals

The trajectory of a marker attached to the finger is a quasiperiodic signal during the finger tapping movement (see section 10). The test characterizing the actual state of neural patients assesses two parameters of the movement: speed and regularity. The regularity of a quasiperiodic signal depends on how close it is to a periodic signal. The periodic signal can have any shape, not only sinusoid. We can characterize how close a quasiperiodic signal is to a periodic signal by breaking it down to basis functions. This can be done by singular value decomposition, SVD analysis [4.22], [4.28]. Let the sampled points of the trajectory of the marker attached to the finger be a row vector y with ℓ elements:

$$y = y(1) \ y(2) \dots y(k) \dots y(l) \quad (4.6)$$

$y(p_i)$ marks the beginning of the i^{th} tapping cycle (when the finger starts to be lifted from the table). The first step is the segmentation of vector y . The beginning of the cycle is when the finger reaches its maximal vertical position. The samples belonging to the i^{th} cycle form a row vector $r(i)$.

$$\begin{aligned} r(1) &= [y(p_1) y(p_1 + 1) \dots y(p_2 - 1)] \\ r(2) &= [y(p_2) y(p_2 + 1) \dots y(p_3 - 1)] \\ &\vdots \\ r(m) &= [y(p_m) y(p_m + 1) \dots y(p_m + c)] \end{aligned} \quad (4.7)$$

The SVD method can handle samples with the same length. It means, $r(i)$ row vectors must have the same number of elements. During finger tapping the cycles do not last for the same time so the length of $r(i)$ row vectors are different. Figure 4.20 shows the trajectories of a healthy person taken during finger tapping. Figure 4.21 shows the trajectories of a Parkinsonian patient. Cycles are aligned at their maximum vertical positions. The number of elements in $r(i)$ row vectors can be assured by resampling. Let the length of resampled row vectors be the median of the lengths of original $r(i)$ vectors, denoted by n .

$$length[r(i)] = \begin{cases} (i < m) : p_j - p_i, j = i + 1 \\ (i = m) : c + 1 \end{cases} \quad (4.8)$$

$$n = median\{length[r(i)]\}$$

Resampling can be done by linear interpolation. The first and last element of each row vector remains unchanged even after resampling: $yr(i,1) = y(p_i)$, $yr(i,n) = y(p(i+1)-1)$. The last row vector is an exception, where $yr(m,n) = y(p_m+c)$. The elements of the resampled row vectors $yr(i,j)$ are interpolated between the original $y(p_i+k-1)$ and $y(p_i+k)$ points, where k is defined by eq. 4.9.

$$k = entier(n/length(r(i)) \cdot j), \quad 2 \leq j \leq n. \quad (4.9)$$

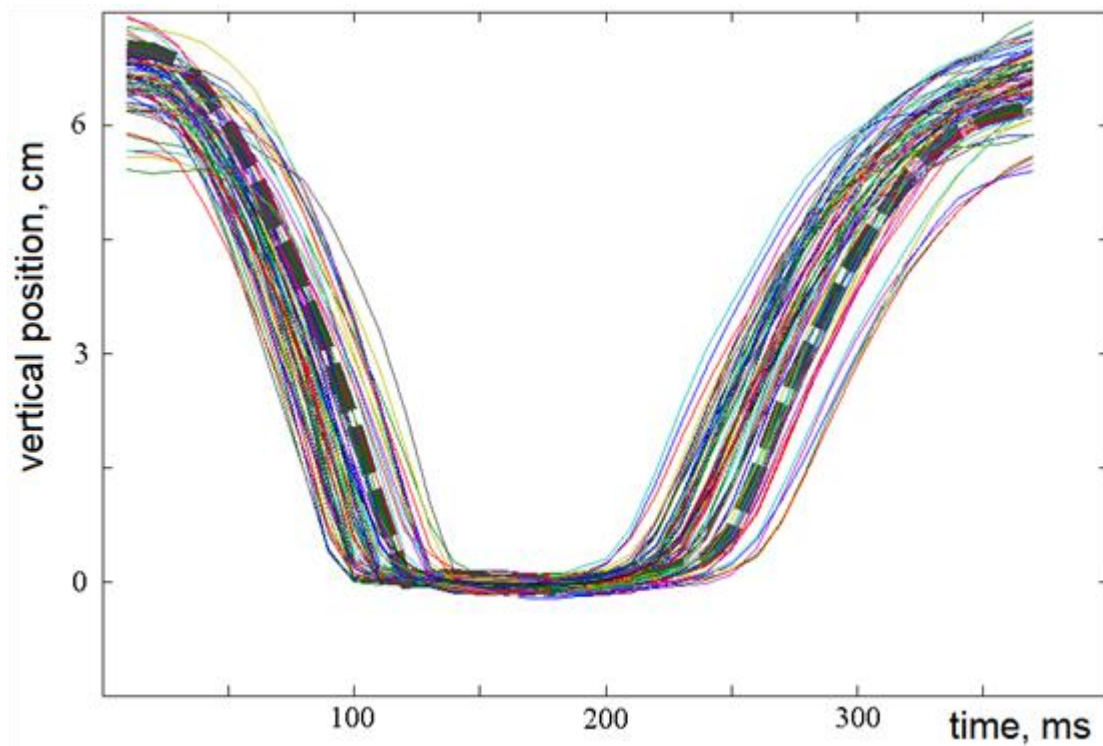
The matrix created in this way is given by eq. 4.10.

$$X = \begin{bmatrix} yr(1,1) & yr(1,2) & \dots & yr(1,n) \\ yr(2,1) & yr(2,2) & \dots & yr(2,n) \\ \vdots & & & \\ yr(m,1) & yr(m,2) & \dots & yr(m,n) \end{bmatrix} \quad (4.10)$$

When the matrix is composed the SVD function of Matlab® (The MathWorks Inc.) is used. This determines the matrices S , V and Σ so that $X = S\Sigma V^T$. A detailed description of the SVD method is given in [4.23]. Σ is a diagonal matrix, its σ_i elements can be regarded as weighting factors of the basis functions that are needed to describe the periods identified in the sampled data y and represented by the row vectors of X . The columns of V can be regarded as basis functions. Adding up the v_j basis functions weighted by $u_i\sigma_i$ we get the i^{th} period of the signal, i.e. the i^{th} row of X . The periodicity of movement (PM) is characterised by the rate of the dominant basis function within all functions necessary to describe the complete record, i.e. all periods. This is calculated on the basis of the diagonals of Σ , σ_i .

$$PM = \frac{\sigma_1^2}{\sum_{i=1}^n \sigma_i^2} \quad (4.11)$$

Figure 4.20. Aligned trajectories of a marker attached to the index finger of a healthy subject (thin solid lines) and the base vector determined by SVD analysis (thick dotted line)



If σ_1 is dominant (σ_i are arranged in decreasing order) then the movement is nearly periodical and the first column of V (v_1) is the dominant basis function. If all σ_i except σ_1 are zero then the movement is strictly periodic, it can be fully described with no more than one base vector. As a result, the parameter value PM equals 1. In case of a nearly periodic movement σ_1 is dominant but further σ_i elements are non-zero. The PM parameter value decreases as further vectors are needed to describe the movement.

Figure 4.21. Aligned trajectories of a marker attached to the right middle finger of a Parkinsonian in Hoehn-Yahr 1 stage (thin solid lines) and the base vector determined by SVD analysis (thick dotted line)

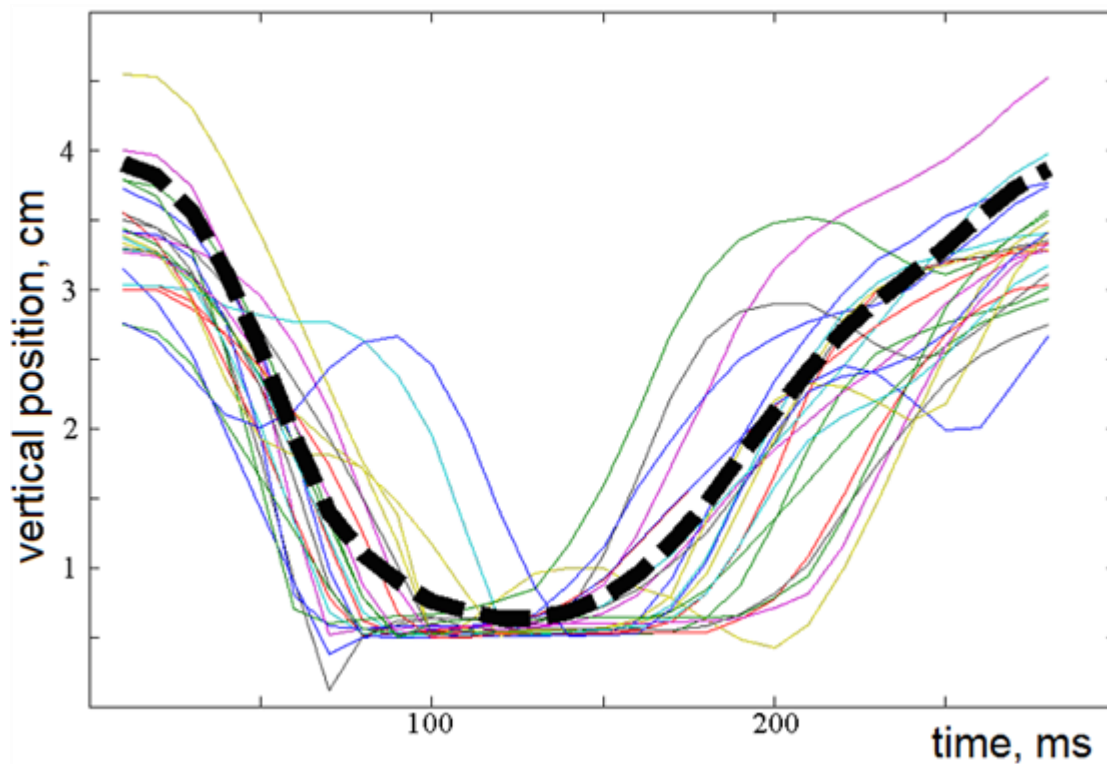


Figure 4.20 and 4.21 show periods of finger movements together with the base vector determined by the SVD method. It is clear that the movement of the young healthy subject is more regular than the movement of the Parkinsonian patient (in Hoehn-Yahr stage 1, i.e. in mild stage). Figure 4.22 and 4.23 show the relative weights of all vectors and the weight of the base vector in different periods determined by SVD analysis for a marker movement during finger-tapping test of a healthy subject (see Figure 4.20) and a Parkinsonian (see Figure 4.21). The figures demonstrate the application of the SVD method to quantify regularity. The dominant base vector has a much higher weight for the complete record in case of the healthy subject than of the Parkinsonian patient. Also, the weight of the dominant base vector has a smaller relative variation (7 ... 9) for the healthy subject than for the Parkinsonian patient (3 ... 5). Parameter PM quantitatively characterizes the finger tapping movement [4.24].

Figure 4.22. The relative weights of all SVD vectors (left) and the weight of the base vector (right) for the 79 cycles of the index finger of a young healthy subject during a 20-s finger-tapping test

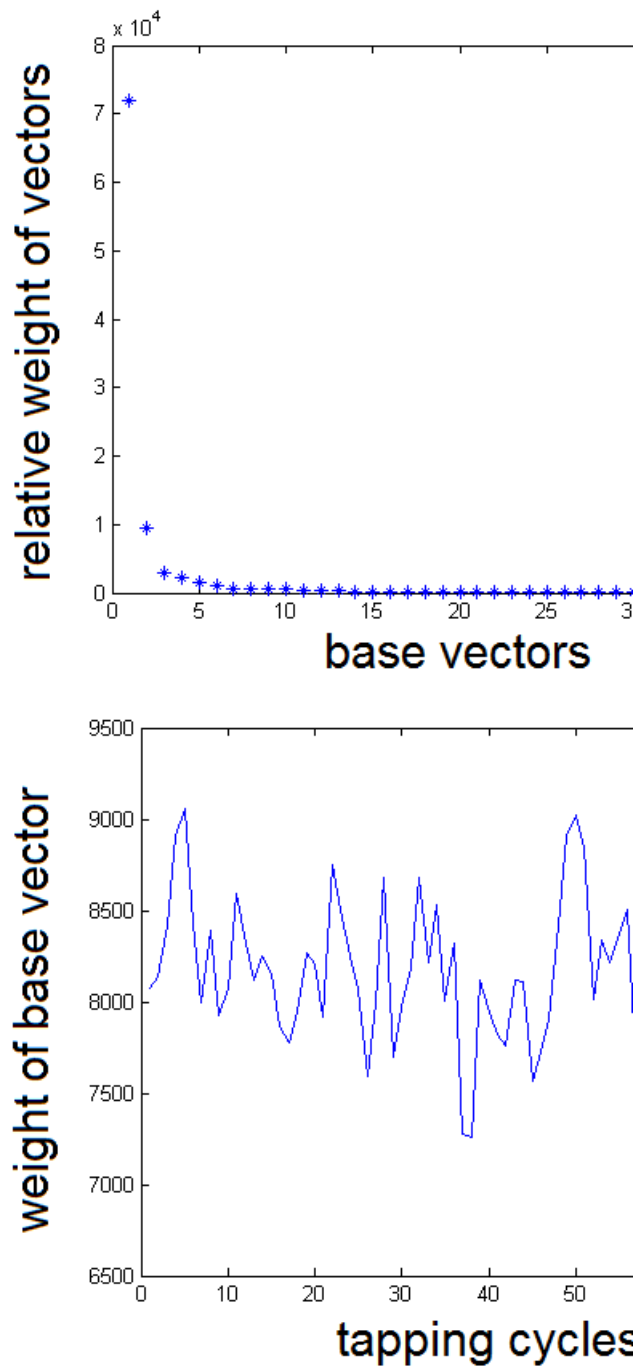
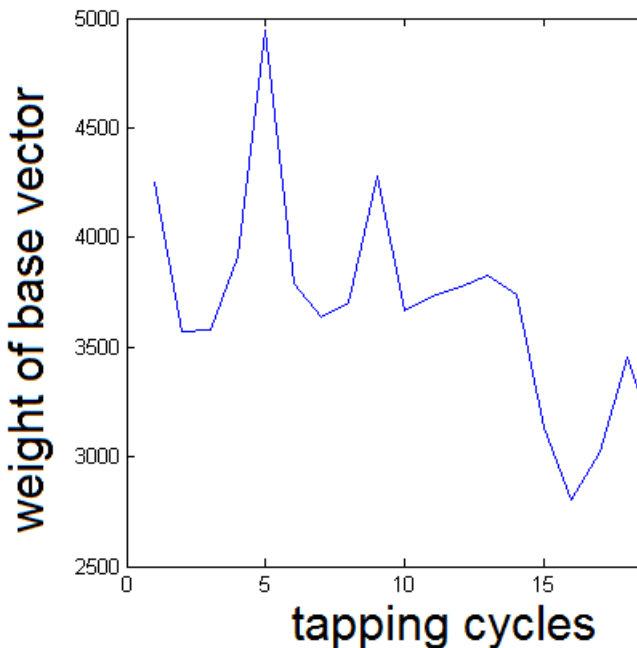
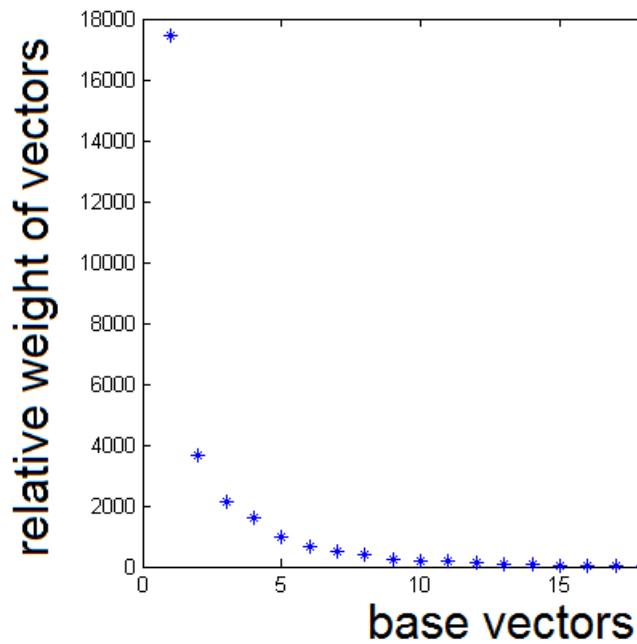


Figure 4.23. The relative weights of all SVD vectors (left) and the weight of the base vector (right) for the 23 cycles of the index finger of a Parkinsonian during an 8-s finger-tapping test



3. Compression of biosignals

In biosignal analysis data compression techniques are of great interest when data transmission (e.g. in telemedicine applications) or long-term recordings (e.g. 24-hour monitoring or intensive care) are involved. Personalized health care is assisted by regular recording of biosignals (e.g. ECG, EEG) and highlighting the changes. These procedures explain the application of data compression.

There are two types of data compression methods: lossless and lossy. The widely used arj, zip programs are lossless. Lossy compression methods are more efficient: the compression rate is higher but the original data can be restored with a given deviation. In case of biosignals the a priori information helps increase the compression rate. The ECG signal has mainly flat segments, only the QRS complex is steep. Instead of the original data the difference of adjacent samples should be stored. The flat parts result in small differences. This allows an efficient variable length coding (short codes for small values).

Turning point (TP) algorithm

Divides the size of the original data set by two. Always examines three points at a time, one is the reference point. The first point in the data set is the first reference point which is stored. Of the next two points one is selected as next reference point and the other is discarded. The new reference is also stored and the next two points are evaluated. The procedure is repeated until the last data point.

Of the two points following the reference point the turning point will be saved. Figure 4.24 shows the selection rule. Three points can be arranged in nine different ways. Two arrangements differ if the relation (smaller, bigger, equal) of adjacent points is different.

Operation $\text{sign}(x)$ is defined by eq. 4.12.

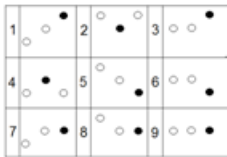
$$\text{sign}(x) = \begin{cases} 0, & \text{if } x = 0, \\ +1, & \text{if } x > 0, \\ -1, & \text{if } x < 0, \end{cases} \quad (4.12)$$

Eq. 4.13 defines how to select the discarded point out of the two points (x_1, x_2) following the reference point (x_0). If the logical expression in eq. 4.13 is 0, then x_1 must be stored (and x_2 discarded) otherwise x_2 must be stored (and x_1 discarded).

$$\text{NOT}(\text{sign}(x_1 - x_0)) \text{ OR } (\text{sign}(x_2 - x_1) + \text{sign}(x_1 - x_0)) \quad (4.13)$$

x_1 must be stored if the slope between $x_1 - x_0$ and $x_2 - x_1$ has opposite sign. The turning point algorithm is simple; the necessary computational capacity is small results in a fix 2:1 compression rate. Its disadvantage is that the output data set cannot be considered as equidistantly sampled.

Figure 4.24. The nine possible arrangements of three consecutive points (x_0, x_1, x_2)



The AZTEC algorithm

The AZTEC (Amplitude Zone Time Epoch Coding) algorithm uses piecewise linear approximation. Starting from a point to be stored (P_e) it calculates the slope (S_i) of the line to each succeeding point (P_i). If at point n the difference between the minimum and the maximum slopes exceeds a predefined value then the line between P_e and P_{n-1} is stored. The procedure is repeated, P_{n-1} will be the next P_e .

Restoring the compressed data needs smoothing (low-pass filtering) at the abrupt slope changes at the connection of lines.

The parameter expressing compression error is given in eq. 4.14.

$$\text{prd} = \sqrt{\frac{\sum_{i=0}^n (x_{\text{original}}(i) - x_{\text{approx}}(i))^2}{\sum_{i=0}^n (x_{\text{original}}(i))^2}} \cdot 100 [\%] \quad (4.14)$$

where prd: percent root-mean-square. A simple formula for filtering is given by eq. 4.15.

$$pk = (-2x_{k-3} + 3x_{k-2} + 6x_{k-1} + 7x_k + 6x_{k+1} + 3x_{k+2} - 2x_{k+3})/21 \quad (4.15)$$

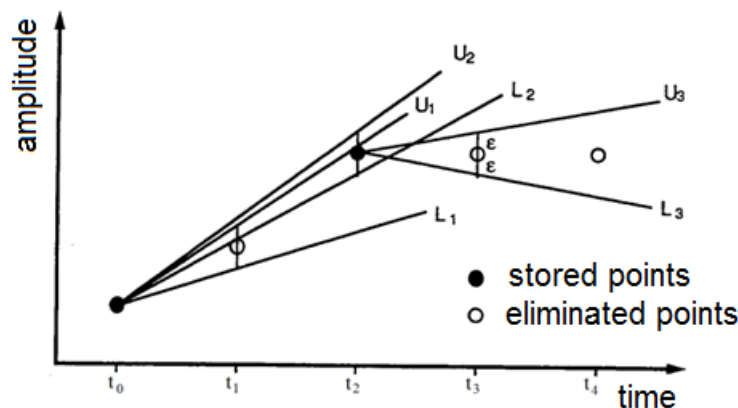
where x_i is the compressed, pi is the filtered data set.

The method has several variations. CORTES (Co-ordinate Reduction Time Encoding System) is a combination of the TP and the AZTEC methods. At flat parts it uses the ZTEC algorithm, at steep parts the TP method.

The fan algorithm

This algorithm uses piecewise linear approximation also. The method is illustrated in Figure 4.25.

Figure 4.25. The FAN algorithm



In Figure 4.25 the error tolerance is denoted by ε . From a stored point two lines are drawn towards the next point. One to the maximum ($x_a + \varepsilon$) and one to the minimum ($x_a - \varepsilon$) allowed value. The two lines form a shape similar to one element of a fan; this explains the name of the method. In Figure 4.25 the first stored point is x_0 at t_0 , the second point is x_1 at t_1 . Line U_1 is the line to $x_1 + \varepsilon$, line L_1 is the line to $x_1 - \varepsilon$. The next point (x_2 at t_2) is within the tolerance set by U_1 and L_1 so x_1 is discarded. Similarly to U_1 and L_1 we draw lines U_2 and L_2 that belong to x_2 . We select the minimum slope of U_i values, and the maximum slope of L_i values. These are U_1 and L_2 forming the new fan. x_3 is outside of this fan, so x_2 must be preserved. x_2 is the new starting point.

Among TP, AZTEC and fan algorithms, the last gives the best signal fidelity with the same compression rate.

4. Problems

The nominal value of the sampling rate of HHMD is 1 kHz. (The video http://project.mit.bme.hu/kobak2012/ECG_PPG.wmv illustrates the recording with HHMD.) The records available at the given web site were made using different devices. The sampling rate of a device may differ from the nominal value by $\pm 1.5\%$. For a given record, the sampling frequency can be determined by regarding the power line frequency being 50.0 Hz. On the web site you can find a description of the data structure of the file and a Matlab program that reads a record.

1. Load the *project.mit.bme.hu/kobak2012/ECGwithbignoise.hhm* file to Matlab. Draw the *ecg1* time function and draw the low-pass filtered time function to the same figure. Evaluate the effect of the parameters of the low-pass filter (type, order, corner frequency) on power line noise suppression and on ECG signal distortion.
2. Load the *project.mit.bme.hu/kobak2012/bpm_patZ1_01.hhm* file to Matlab. Determine the dominant frequency of noise during inflation analysing cuff pressure time function (press).
3. Determine how cuff pressure influences the delay time between time functions *ecg1* and *ppgl_nir* in the record *project.mit.bme.hu/kobak2012/bpm_patZ2_01.hhm*. Delay time is defined in between the S point of ECG and local minimum of PPG. Determine the cuff pressure when the change in delay time is maximum.
4. Determine the cuff pressure when pulsation ceases in the *ppgl_nir* time function of the file *project.mit.bme.hu/kobak2012/bpm_patZ2_01.hhm*. This is the systolic pressure.
5. Determine the breathing frequency of the tested person based on the record in the file *project.mit.bme.hu/kobak2012/bpm_patZ1_01.hhm*.
6. Determine the change of the momentary heart frequency during blood pressure measurement analysing the *ppgl_nir* time function of the file *project.mit.bme.hu/kobak2012/bpm_patZ2_01.hhm*.

From the file *project.mit.bme.hu/kobak2012/bpm_yhf01_01.hhm* draw the ECG and PPG signals belonging to two heart cycles.

7. Load the file *project.mit.bme.hu/kobak2012/bpm_patZ2_01.hhm* to Matlab. Apply third order Butterworth low-pass filter with corner frequency $f_0 = 10\text{Hz}$ to *ecg1*. Compare the functions 'filter' and 'filtfilt'.
8. Increase the corner frequency in Problem 8 to $f_0 = 25\text{Hz}$ and evaluate the difference.
9. To increase the signal-to-noise ratio in of *ecg1* in Problem8 apply a third order Butterworth band-stop filter ($f_0 = 50\text{Hz}$). Evaluate the result.
10. Load the file *project.mit.bme.hu/kobak2012/bpm_stops_during_deflation_shm01_01.hhm* to Matlab. Select one heart cycle from the first 24 s and determine the time delay (ΔT_{EP}) between the start of the pulse wave (S point of ECG) and its arrival to the fingertip (start of rise in PPG). Estimate the pulse wave velocity, supposing the distance between left ventricle and fingertip is 90 cm.
11. Analyse how ΔT_{EP} time (according to problem 11) changes when cuff pressure increases.
12. Load the file *project.mit.bme.hu/kobak2012/bpm_yhf01_01.hhm* to Matlab. Calculate the mean value and standard deviation of t_{RR} values of *ecg1*.
13. Load the file *project.mit.bme.hu/kobak2012/bpm_yhf01_01.hhm* to Matlab. Calculate the mean value and standard deviation of t_{QT} values of *ecg1*.
14. Load the file *project.mit.bme.hu/kobak2012/bpm_yhf01_01.hhm* to Matlab. Calculate the mean value and standard deviation of t_{PQ} values of *ecg1*.
15. Load the file *project.mit.bme.hu/kobak2012/bpm_yhf01_01.hhm* to Matlab. Calculate the mean value and standard deviation of QRS amplitudes.
16. Load the file *project.mit.bme.hu/kobak2012/bpm_yhf01_01.hhm* to Matlab. Calculate the mean value and standard deviation of the width of QRS complexes.
17. Load the file *project.mit.bme.hu/kobak2012/bpm_yhf01_01.hhm* to Matlab. Improve the signal-to-noise ratio by averaging. Align the heart cycles at the R peaks.
18. Load the file *project.mit.bme.hu/kobak2012/bpm_yhf01_01.hhm* to Matlab. Determine the cuff pressure value when pulsation ceases in *ppgl_nir*.
19. Load the file *project.mit.bme.hu/kobak2012/bpm_patZ2_01.hhm* to Matlab. Complete FFT analysis on the *ecg1* signal using 10-s window and sliding it along by 5-s steps. Draw the spectra one behind the other.
20. Repeat the analysis of problem 20 using 20-s window and 4-s step.
21. Load the file *project.mit.bme.hu/kobak2012/bpm_patZ2_01.hhm* to Matlab. Plot the amplitude change of oscillometric pulses in cuff pressure (press) versus cuff pressure.
22. Load the file *project.mit.bme.hu/kobak2012/bpm_patZ2_01.hhm* to Matlab. Plot the maximum slope of oscillometric pulses versus cuff pressure.
23. Load the file *project.mit.bme.hu/kobak2012/bpm_yhf01_01.hhm* to Matlab. Determine the breathing frequency from the ECG signal (*ecg1*).
24. Load the file *project.mit.bme.hu/kobak2012/bpm_stops_during_deflation_shm01_01.hhm* to Matlab. Draw the frequency spectrum of ECG and *ppgl_nir* one below the other. Based on them, determine the breathing frequency.

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Chapter 5. Safety

Electronic devices are used to test patients as well as to assure their comfort. Failure or misuse of electronic devices is a danger to both patients and medical staff. Prevention of accidents includes design, manufacturing, application and maintenance according to standards [5.2]. Most of these are IEC (International Electrotechnical Commission) standards [5.12]. This chapter would like to draw attention to the importance of related standards which are often updated. Engineers must be familiar with the principles of safety. Electrical safety in hospitals got into focus following Ralph Nader's paper (Ladies Home Journal, April 24, 1970), [5.1]. The paper claimed that 1200 American died yearly in hospitals as a result of electrocution during routine diagnostic or therapeutic procedure. In this chapter we concentrate on the protection against electric shock. Several biomedical equipment require Uninterruptible Power Supply (UPS) to maintain the patient's vital function (e.g. a medical ventilator to mechanically move breathable air into and out of the lungs). Although it can be indispensable for the patient's safety UPS is out of the scope of this book.

1. Physiological effect of electric current

Electric current stimulates nerves and muscles, heats up tissues even beneath the skin [5.2], [5.3], [5.4]. The effect and danger of current depends on several factors.

The current path. The most dangerous is when current flows through the heart, lung and brain.

The duration of impact. Current that flows through the patient for 0.5 – 1 s is much less dangerous than longer impacts.

The frequency of the current. For humans the most dangerous is the current with 50 – 60 Hz (i.e. around power line) frequency. The effect of current with frequency below 10 Hz is reduced. DC current with 3 ... 5 times higher effective value has the same effect as 50 Hz current. If DC current flows through the body for a long time, electrolysis may demolish the cells. When the frequency is above 1 kHz the current density is largest to the body surface (skin effect) and so it avoids organs.

The magnitude of the current. Figure 5.1 shows the typical current ranges that have different physiological effects under given conditions.

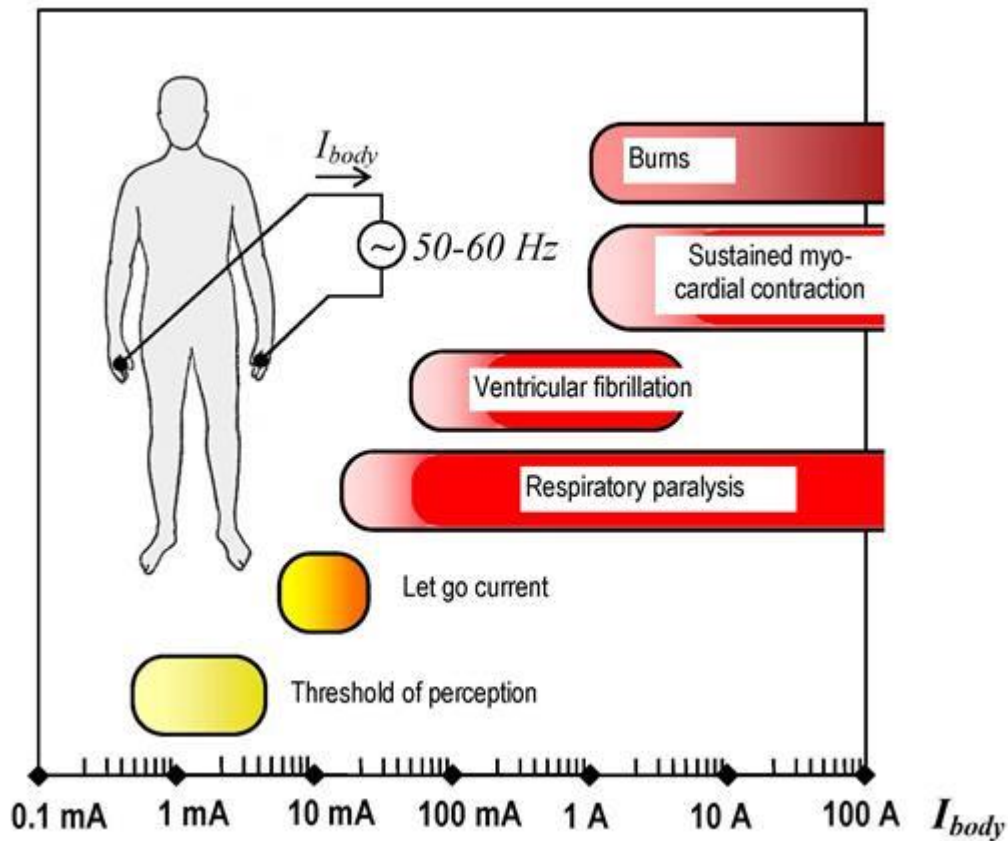
Around the threshold of perception the current causes tingling. When the current exceeds the 'let go' limit the person is unable to go against its contractive effect (release the wire). Based on measurements for 99% of women this limit is estimated to be within 6 – 15 mA. The same range for men is 8 – 23 mA. Stronger current causes pain, contraction of breathing muscles, respiratory arrest. The current flowing through the heart disturbs its electrical operation. If ventricular fibrillation occurs then blood flow ceases. This is a fatal threat because fibrillation subsists even after the electric current (that evoked it) ceases. Further increase of the current causes the contraction of the whole heart muscle. Blood flow stops but it is likely to start flowing again when the current ceases. The heating effect of current first burns the skin around the entry points.

Personal properties are responsible for the variation of ranges. These are: gender, age, weight, body shape (corpulent, underweight, tall, etc.), physical and mental state, but also the actual mood. The current flowing through the body is given by eq. 5.1.

$$I_{\text{body}} = \frac{V_a}{R_{\text{body}}} \quad (5.1)$$

R_{body} varies from person to person. The actual condition of the skin (dry, sweaty, injured) and the contact area greatly influences it. The skin – because of its relatively high impedance – easily breaks down within one second when it contacts with power line voltage. As a result, safety calculations are based on 500 – 1000 Ω total resistance between two limbs.

Figure 5.1. Physiological effects of 50 Hz current flowing for 1-3 s arm-to-arm of a 70 kg male

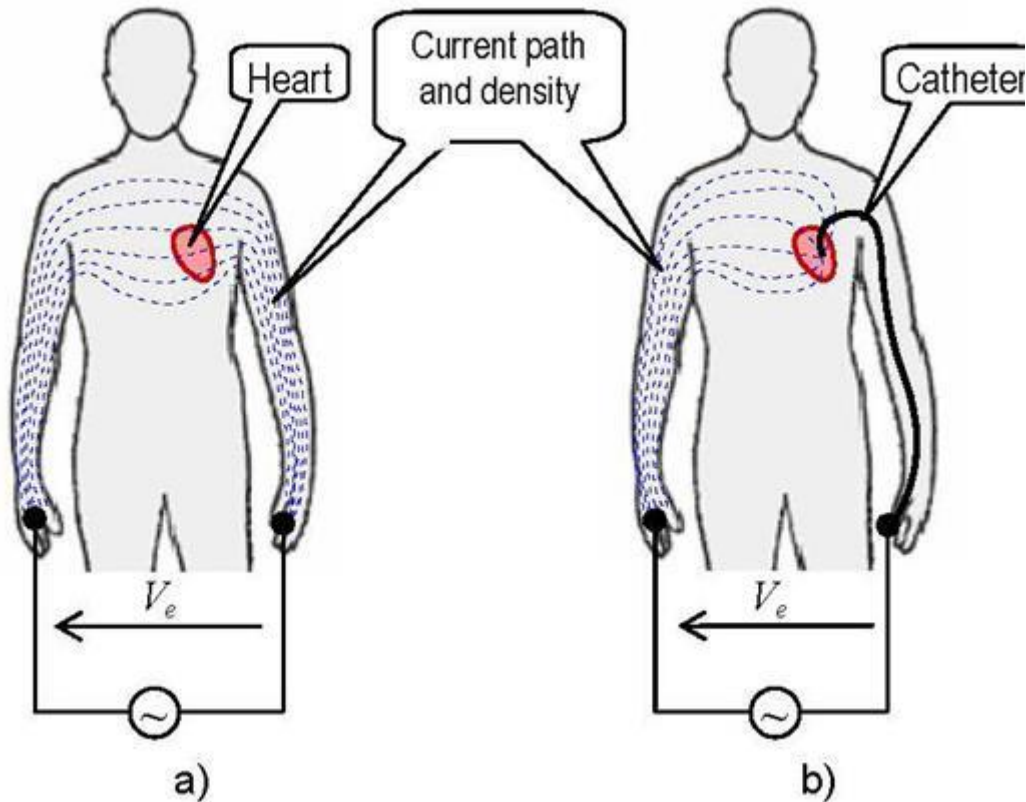


Macroshock and microshock

Macroshock is when the current flows between two points on the body surface (e.g. arm-to-arm or arm-to-foot). The most important factor is the effective value of the current. Everyday electric shock is usually macroshock. In Figure 5.2.a current flows through a large area around the heart. The current ranges given in Figure 5.1 refer to such a situation. During certain treatments one electrode is in the heart or in the blood stream, e.g. in a catheter. This results in a concentration of current path (Figure 5.2.b) flowing directly through the myocardium. This may cause microshock. Patients with a direct current path to their heart are usually in worse physical condition than healthy subjects. The current limit in this case is 10 μ A. This is the maximum current allowed as input current of electronic devices being in direct connection with patients. Even in case of failure the maximum input current must not exceed 50 μ A. This is about one hundredth of the limit of sensation when current flows arm-to-arm; and one tenth of the touch current!

Leakage current flows through the insulation even without failure. Increasing the insulation resistance is not enough to limit leakage current which is determined by the capacitance of the insulation. If the capacitance is 138 pF between a grounded surface and the hot wire of the power line then a 50 Hz current with 10 μ A amplitude will flow. 138 pF is the capacitance between two metal plates of A/4 size being 4 mm far from each other. The resistance of the insulation decreases if its surface is contaminated or dewy.

Figure 5.2. Macroshock (a) and microshock (b). Microshock means that current flows through the heart across small area.



2. Protection against electric shock

Figure 5.3.a illustrates a possible macroshock [5.5], [5.6]. The device is not connected to the protective earth and a short circuit develops between the primary winding of the mains transformer and the core. The core is mounted to the metal chassis so the person touching the device gets electric shock. The current is determined by the power line voltage, resistance R_{body} and resistance to ground (through the shoes and floor) R_{sf} . Suppose $R_{\text{body}} = 1 \text{ k}\Omega$, $R_{\text{sf}} = 1 \text{ k}\Omega$, then the resistance of the wire can be neglected. Eq. 5.2 gives the current value.

$$I_{\text{body}} = \frac{280 \text{ V}}{2 \text{ k}\Omega} = 115 \text{ mA} \quad (5.2)$$

The circuit breaker does not discontinue this electric current which can be lethal. Figure 5.3.b shows, what the use of protective earth (PE) is connecting the metal chassis to ground. Should the same short circuit develop as in Figure 5.3.a, the current between hot wire and ground is determined by the resistance of the wire and the resistance of grounding (R_{PE}). R_{PE} is less than 1Ω thus the current will be much higher than the threshold level of the circuit breaker. The circuit breaker will cut off the current higher than five times its nominal current (I_n) in less than 0.2 s. If someone touches the chassis the voltage there will be $5 \times I_n \times R_{\text{PE}}$.

There are three IEC (International Electrotechnical Commission) protection classes depending on the protective earth connections.

Class I. (Figure 5.4.a.) Active circuit parts are isolated from the touchable conductive parts. The touchable conductive parts are connected to the protective earth which is marked by:



The mains connector must have protective earth pin. The maximal voltage of the touchable conductive parts is determined by the maximal current of the circuit breaker and the resistance of the wire and the protective earth. Current greater than that will cause the circuit breaker cut off the power voltage [5.9], [5.10], [5.11].

Figure 5.3. Macroshock resulting from a short circuit of the mains transformer when the device chassis is not connected to protective earth (a). The same short circuit gets the circuit breaker discontinue the current when the chassis is connected to protective ground (b). Red line shows the current path.

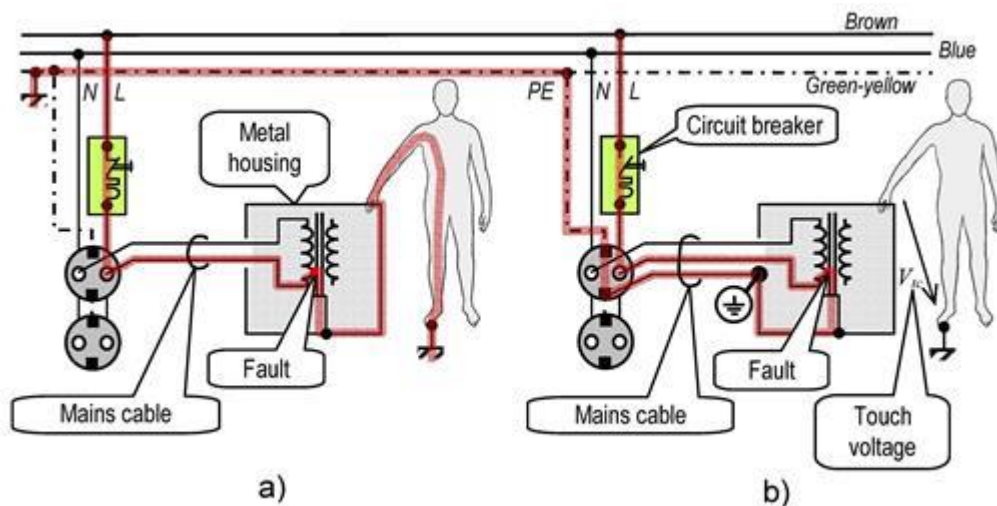
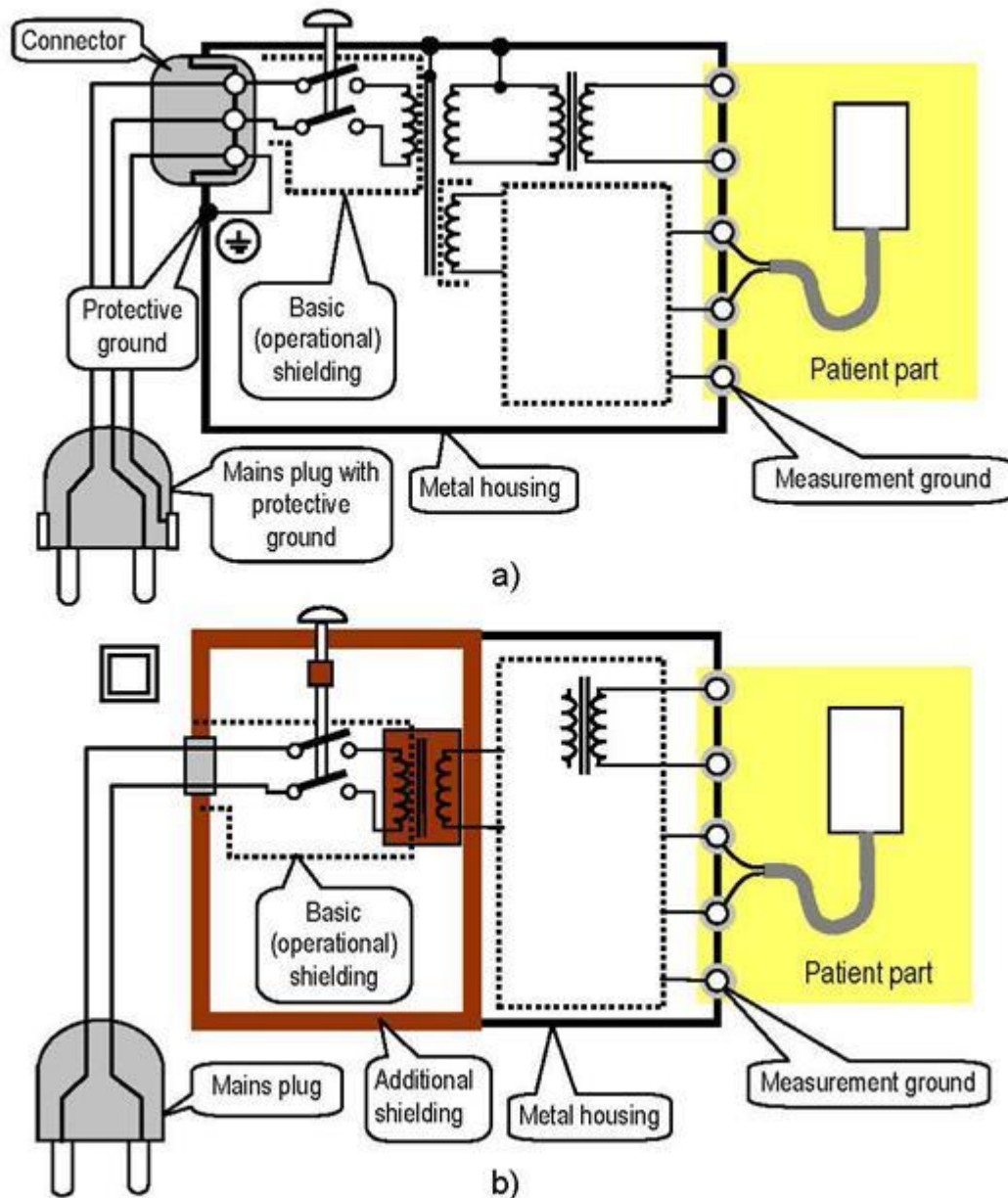


Figure 5.4. The scheme of devices with class I (a) and class II (b) protection classes



Class II. (Figure 5.4.b.) The device has an operation insulation and additional protection insulation (double insulation or reinforced insulation). Single failure must not result in dangerous voltage on the touchable conductive parts without relying on an earthed metal casing. Its symbol is:



Class III.

Devices in this class operate from extra low voltage (ELV). ELV must be smaller than $50 V_{eff}$. The separated extra low voltage (SELV) is defined by IEC: "an electrical system in which the voltage cannot exceed ELV under normal conditions, and under single-fault conditions, *including* earth faults in other circuits". IEC 60601-1 uses the term applied part to refer to the part of the medical device which comes into physical contact with the patient in order for the device to carry out its intended function.

Figure 5.5. Symbols of protection against electrical shock. B (body), BF (body floating), CF (cardiac floating). Patient side of BF and CF devices is galvanically isolated from the mains, floating.



Symbols of different Class III protection types are given in Figure 5.5 f7]. Different leakage current limits belong to the three types both in normal operation and in case of a single fault. IEC 60601-1 is the international medical electric safety standard. The term "Applied Part" refers to a part of a medical device which may come in physical contact with the patient during its normal operation. Applied parts are classified into three types.

Type B applied parts. The least stringent classification. These applied parts are normally not conductive and the patient can immediately release them. Examples are: LED operating lighting, medical lasers, MRI body scanners, hospital beds.

Type BF applied parts. This classification is generally used for applied parts that have conductive contact with the patient, or having medium or long term contact with the patient. Circuits in connection with the patient are floating; galvanically isolated from the power line. Examples are: ECG monitors, incubators and ultrasound equipment.

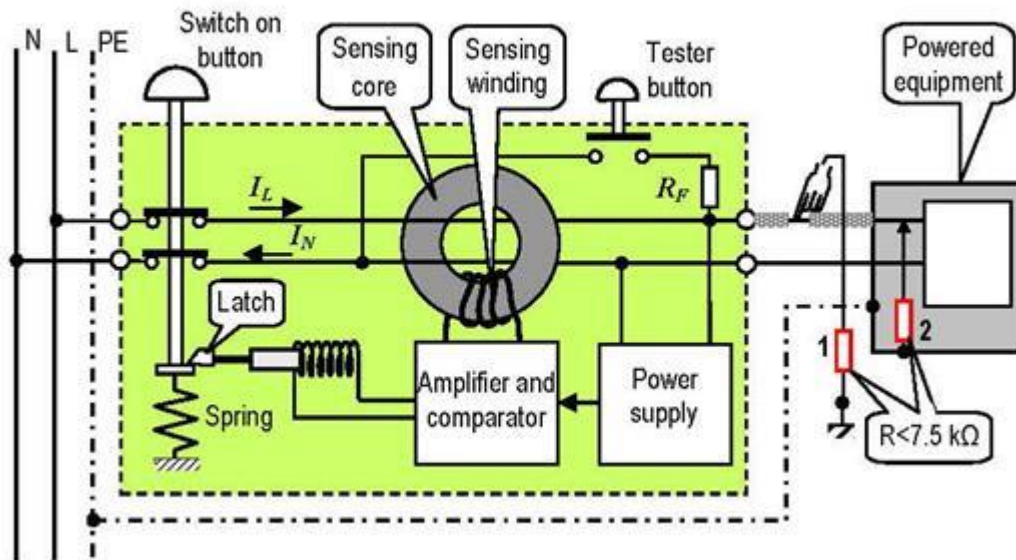
Type CF applied parts. The most stringent classification. It is used for applied parts that may come in direct contact with the heart, such as dialysis machines or invasive blood pressure monitors. Circuits in connection with the patient are floating. The limits for leakage current are below the microshock limit both during normal operation and in case of a single fault.

Residual current devices (RCD). (Also called residual-current circuit breaker (RCCB), ground fault (circuit) interrupter (GFI or GFCI), appliance leakage current interrupter (ALCI), "safety switch", "trip" or "trip switch" [5.9], [5.11].) Figure 5.6 shows the schematic of RCD.

The live connector (L, hot wire) and the neutral connector (N, ground) are led through a differential transformer (ring shaped core). When the leakage current is zero there is no difference between the current flowing through the live conductor and that returning through the neutral conductor. Leakage current (e.g. a person touching a live component in the attached appliance) causes an imbalance in the currents: $I_L \neq I_N$. This results in a magnetic flux inducing voltage in the sense coil. When the leakage current causes an imbalance greater than the nominal value of the RCD ($\Delta I = I_L - I_N$, usual values for biomedical applications are 6 mA, 10 mA, 30 mA) the sense circuitry pulls the bolt and the contacts are forced apart by a spring, cutting off the electricity supply to the appliance. The supply can be switched on again only manually. The test button causes leakage current, pushing this button must cut off electricity supply.

As a general rule only one device should be connected to an RCD. Otherwise even a minor fault of a device cuts off electrical supply of all devices connected to the same RCD. Equipment of vital importance (e.g. positive pressure ventilators) must not be supplied through RCDs.

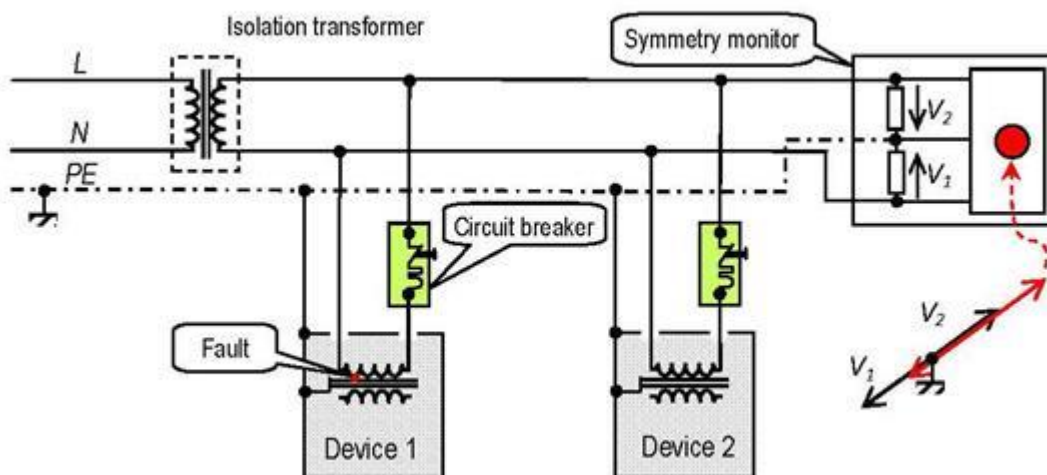
Figure 5.6. Schematic of an RCD. The device cuts off electricity supply when leakage current is caused by either human touch (1) or isolation fault (2). The RCD does not sense short circuit between L and N wires.



3. Line isolation monitor

The line isolation monitor is a device which continually monitors the impedance (resistance and capacitance) from the isolated line to ground and indicates what current could flow to a patient of body resistance 1000Ω , should the patient come into contact with a line conductor (i.e. defective equipment). (Devices exist for three-phase electric supply where all three lines are monitored.) Operating rooms or intensive care units often have isolated electrical power.

Figure 5.7. Devices with isolated power. A single fault in the power line does not cause big short circuit current and the devices continue operation. The line isolation monitor senses the fault and gives an alarm signal.



The line isolation monitor gives an alarm without cutting off electricity supply in case of a single fault (short circuit between isolated line and ground) which does not cause electrical shock. Thus the fault can be fixed before it would have caused shock. The monitor also helps avoid sparks resulting from a single fault. In the operating room the spark could cause explosion because of the anaesthetic gas.

4. Testing electrical biomedical equipment

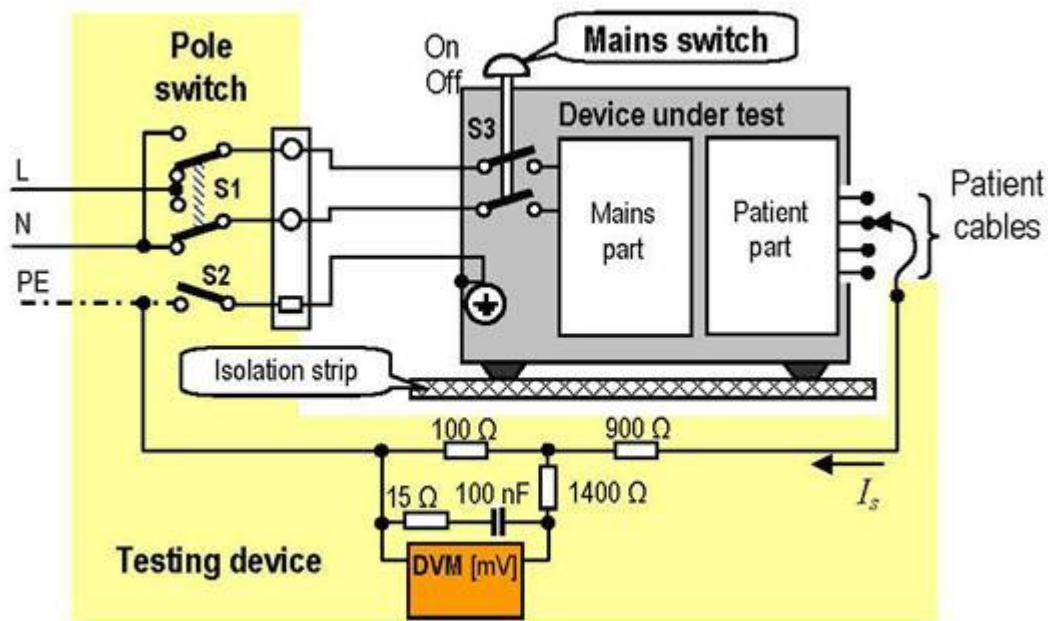
4.1. Safety check

IEC 60601 is a series of technical standards for the safety and effectiveness of medical electrical equipment, published by the International Electrotechnical Commission. First published in 1977 and regularly updated and restructured, as of 2011 it consists of a general standard, about 10 collateral standards, and about 60 particular standards. The standard is an important legal source, too. Should a biomedical equipment cause any health damage the standard helps determine the liability. A device type must be qualified by an accredited institute before production and marketing. In this chapter only application tests are dealt with [5.13], [5.14], [5.15]. These tests are mandatory within predefined periods and also following repair. Tests must be performed according to the users' manual, service manual and the related standards. These documents must be available on the spot.

The status of housing and operator controls as well as the entireness of cables and isolation must be surveyed. The connection to PE must be measured (resistance should be $<0.2\ \Omega$). Isolation (parts connected to power line $>20\text{M}\Omega$, patient part $>50\text{M}\Omega$) and/or breakdown test (1-3 kV) is necessary. Leakage current to ground must be tested (to protective earth $<500\mu\text{A}$, to chassis $<100\ \mu\text{A}$, to patient $<10\ \mu\text{A}$).

Figure 5.8 shows the patient leakage current test according to the standard. The frequency spectrum of the leakage current can span over high frequencies resulting from harmonics of the power line or the switching power supply. The low-pass filter before measuring the voltage of the current-voltage converter by the DVM filters the high frequency components similarly to the human body. The standard does not specify the parameter values and does not let the user select the measurement set-up. The set-up is specified in detail and the results shown by devices must be compared to given limits. This assures the reproducible and comparable results.

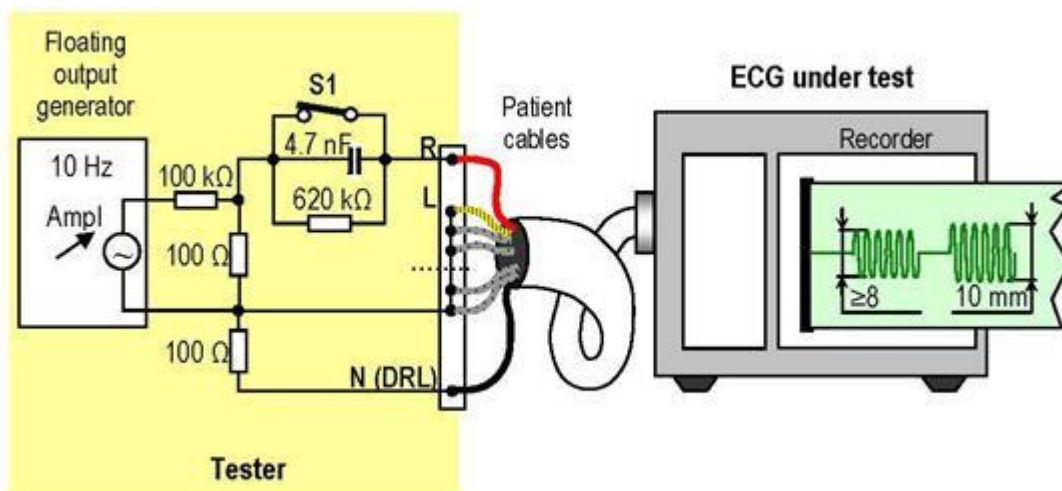
Figure 5.8. Testing the patient part leakage current. I_s leakage current is determined by measuring the voltage it produces across a $100\ \Omega$ resistor. DVM measures the voltage after low-pass filtering similar to the filtering effect of the human body. Test must be repeated on all patient connections setting S1, S2 and S3 switches to all possible states.



4.2. Functional test

Following safety check the functional parameters of biomedical instruments should also be checked. Figure 5.9 shows the test specified in the IEC 601-1 standard for the input impedance of ECG equipment. The measurement set-up is similar to the real application of the device. First the S1 switch is closed and the output voltage amplitude is set so that the ECG displays 10 mm peak-to-peak. The drop in the amplitude of the output signal should not be higher than 20% when the series impedance ($620\text{ k}\Omega$ and 4.7 nF in parallel) and the input impedance divides the input voltage (S1 open). This is equivalent to a minimum of $2.48\text{ M}\Omega$ input resistance. If this minimum were specified, users could measure it using inappropriate method (e.g. trying to measure I_{input} and V_{input} directly).

Figure 5.9. Testing the symmetrical input impedance of an ECG device. First S1 switch is closed and the floating output generator is set so that the output registration show 10 mm peak-to-peak. Then S1 switch is opened. Input impedance is acceptable if the peak-to-peak registration does not drop below 8 mm.



5. Electromagnetic compatibility

Electric devices should not disturb each other. However, they influence each other. Even atmospheric and weather effects have an impact on electric devices. Electromagnetic compatibility (EMC) summarizes these effects and specifies the allowed disturbance [5.16], [5.17], [5.18].

EMC has two kinds of requirements for a device:

- immunity (disturbance tolerance) towards external effects,
- limiting its own disturbance emission.

Standards contain limits so that emission is smaller with a sufficient reserve than tolerance.

The following external disturbances should be taken into account while analysing immunity:

- Electrostatic discharge, ESD. Typical occurrence when the person walking on isolated floor charges up and when touches the equipment discharges.
- Switching transients, which occur usually in the power line system and get into the device through the power supply or through the long cables.
- Radiofrequency noise emanating from radio stations and GSM telephone systems.
- Effect of lightning in the power line system.
- Changing electromagnetic field caused by electric devices nearby.

The above enlisted noises have to be simulated by standard inspection methods which require special devices. The allowed effects of external disturbances are also classified.

- As a result of disturbance operation may stop but it must be able to be restarted (no permanent fault).
- As a result of disturbance the operation can be faulty for a while but the device returns to normal operation without restarting.
- The disturbance is not allowed to cause drop-out, not even a measurement error greater than a predefined limit.

Disturbance can propagate by radiation or by conduction. This applies for both emission and immunity. Testing conducted disturbances must be added to or taken from the signal lines with defined filters in the 150 kHz – 80 MHz range (this range changes every now and then as a result of development). The frequency range of the radiated noise is above the conducted disturbance range up to 2 GHz. Test of radiated noise requires very expensive shielded room, antennas, transmitters and receivers.

To meet the EMC specifications careful development (including the wiring of the PCB) and application of protection elements (noise filters and suppressors, shielding, overvoltage shunts) are needed. Their effective operation must also be tested.

6. Problems

1. The nominal current of the circuit breaker in Figure 5.3.b. is $I_n=6$ A. (I_n is passed through permanently.) Current $I_v=5I_n$ is cut off within $t<200$ ms. Calculate the maximum resistance of the protective earth R_{PE} to keep the touch voltage below 50 V. The resistance between the touchable metal chassis and protective earth is $R<0.2\ \Omega$.
2. The RCD in Figure 5.6 is tested by pushing the test button. Calculate the value of the resistance R_F to test the RCD with $I_{DN}=10$ mA nominal current.
3. Calculate the voltage shown by the DVM in Figure 5.8 when the leakage current is $I_s=10\ \mu\text{A}$, its frequency is 50 Hz. The DVM should be set in DC or AC mode?

4. What is the role of the 100 nF capacitor in the measurement set-up in Figure 5.8? Calculate the frequency range where the roll-off is -20 dB/decade.
5. The input impedance of an ECG device is tested according to Figure 5.9. Calculate the input impedance if the peak-to-peak output changes from 10 mm to 9 mm when S1 is switched off. Analyse the impedance of the 4.7 nF capacitor in parallel with the 620 kΩ resistor and the input capacitance (~200 pF) at the 50 Hz frequency: are they negligible?

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Attention! Safety instructions and standards may vary from country to country. The standards in the references are not necessarily valid in each country. Always the standards in effect must be used.

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Chapter 6. The electrical activity of the heart

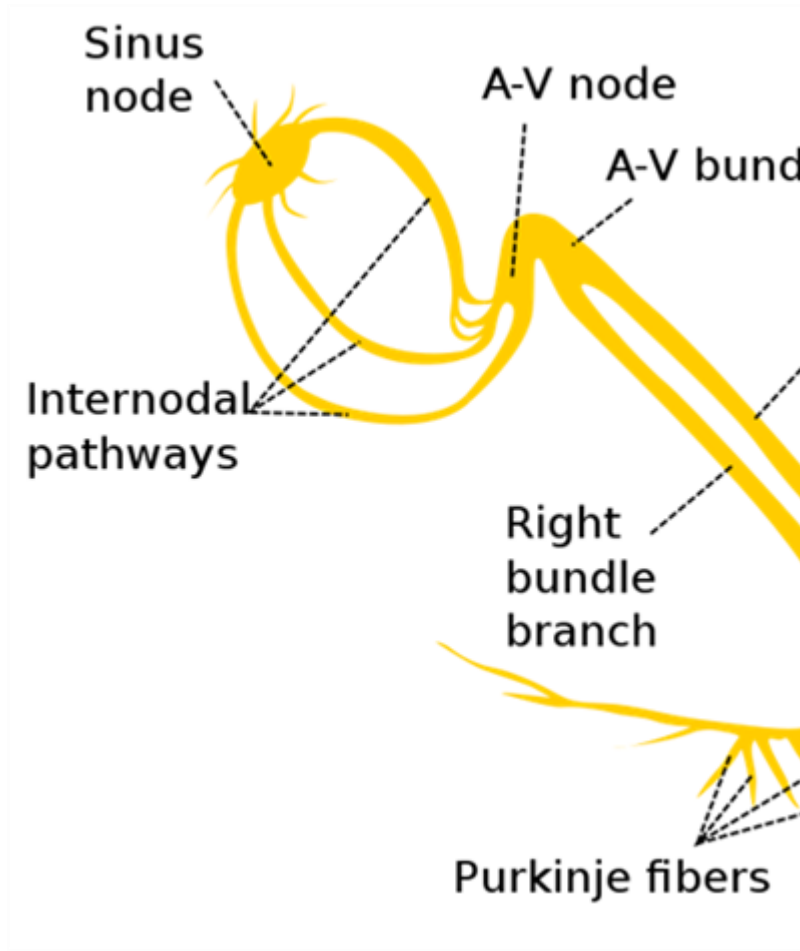
1. Origin of the ECG signal

The physiological basics of the heart are given in [6.1], [6.2], [6.3]. It has four chambers; it keeps the blood flowing in the body (pumping function). Heart muscle comprises about one million cells. Their coordinated contraction and relaxation is needed to pumping the blood. In the upper corner of the right atrium is the sinoatrial (SA) node. It comprises pacemaker cells. Their threshold level changes thus they provide 40 ... 200 electrical impulses (action potentials) per minute. In the resting state the interior is at -70 mV compared to the exterior of the cell. Following excitation (when external charges force the membrane potential above -55 mV) the interior abruptly changes to $0 \dots +20$ mV to the exterior of the cell. The depolarized state is instable, after a few milliseconds most of the cells revert back to resting (polarized) state. The depolarization and polarization again is called action potential. During most part (called refractory period) of the action potential the cell neglects further excitations. Heart muscles have a 200 – 300 ms long action potential with nearly so long refractory period. Pulses emanating from the SA node propagate along the nerves depolarizing the cells of heart muscle. Polarization and repolarization result in the autonomous functioning of the heart. The timing of the action potential propagation and depolarization controls the pumping function of the chambers.

Figure 6.1. Human heart after autopsy.
(<http://commons.wikimedia.org/wiki/File:Humhrt2.jpg>, author: Stanwhit607)



Figure 6.2. Propagation of excitation throughout the heart
http://commons.wikimedia.org/wiki/File:Electrical_conduction_system_of_the_heart.svg
author:Madhero88



Autonomous functioning of the heart is certified by the fact that it keeps on contracting and relaxing in an adequate solution (with enough oxygen) for hours even after being removed from the body. The widely known demonstration can last for hours with frog's or turtle's heart. Figure 6.1 shows a human heart after autopsy while Figure 6.2 shows the nerves along which excitation propagates. Depolarization and repolarization result in the potential changes measured on the body surface as ECG signal. The propagation of depolarization is illustrated by the animation available at http://project.mit.bme.hu/kobak2012/depolarization_in_the_heart.pps

The action potential propagation velocity is different along the heart. Typical values are [6.2]:

sinoatrial node	<0,01 m/s,
atrial tissue	1–1,2 m/s,
AV node	0,02–0,05 m/s,
bundle of His	2–4 m/s,
bundle branches	2–4 m/s,
Purkinje fibres	2–4 m/s,
ventricular tissue	0,3–1 m/s.

Figure 6.3 shows what can be measured in the axon of a nerve cell when an action potential passes by. One electrode is inside the cell, the other is outside. The experiment can be done with the giant axon of a squid which can have 1 mm diameter. This allows insertion of a microelectrode.

Figure 6.3. Potential difference between the interior and exterior of a tube like cell during action potential

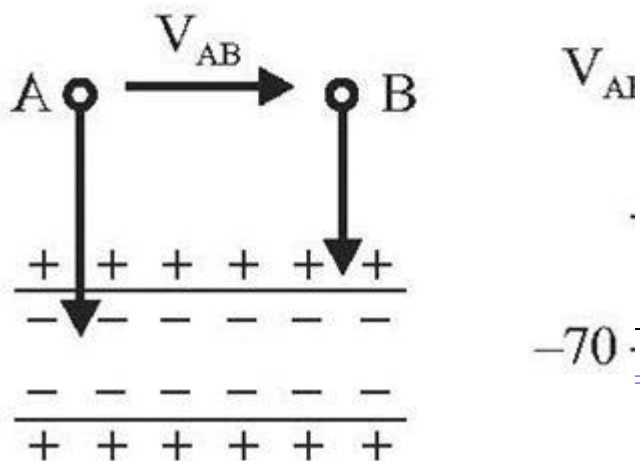
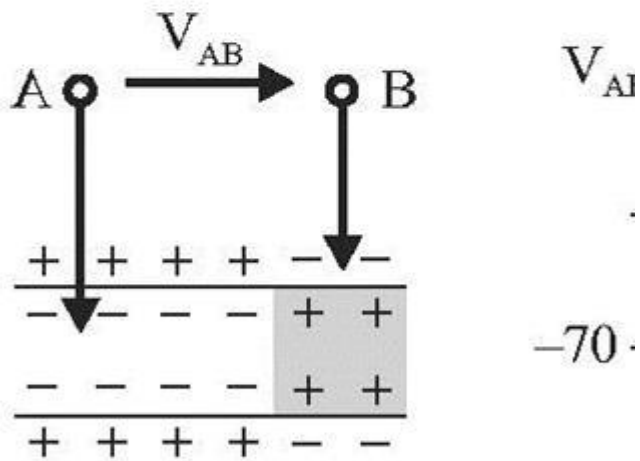
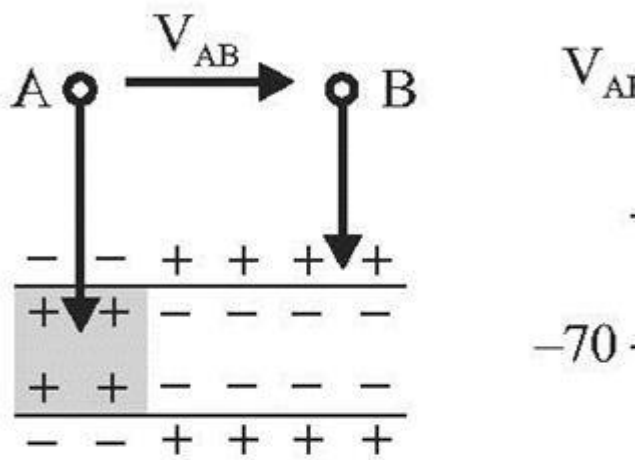
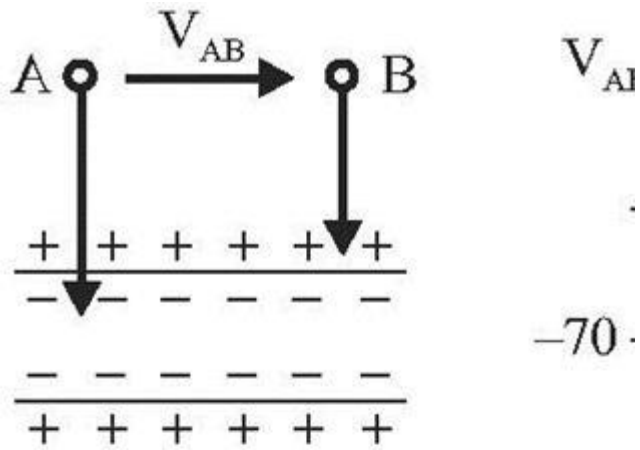
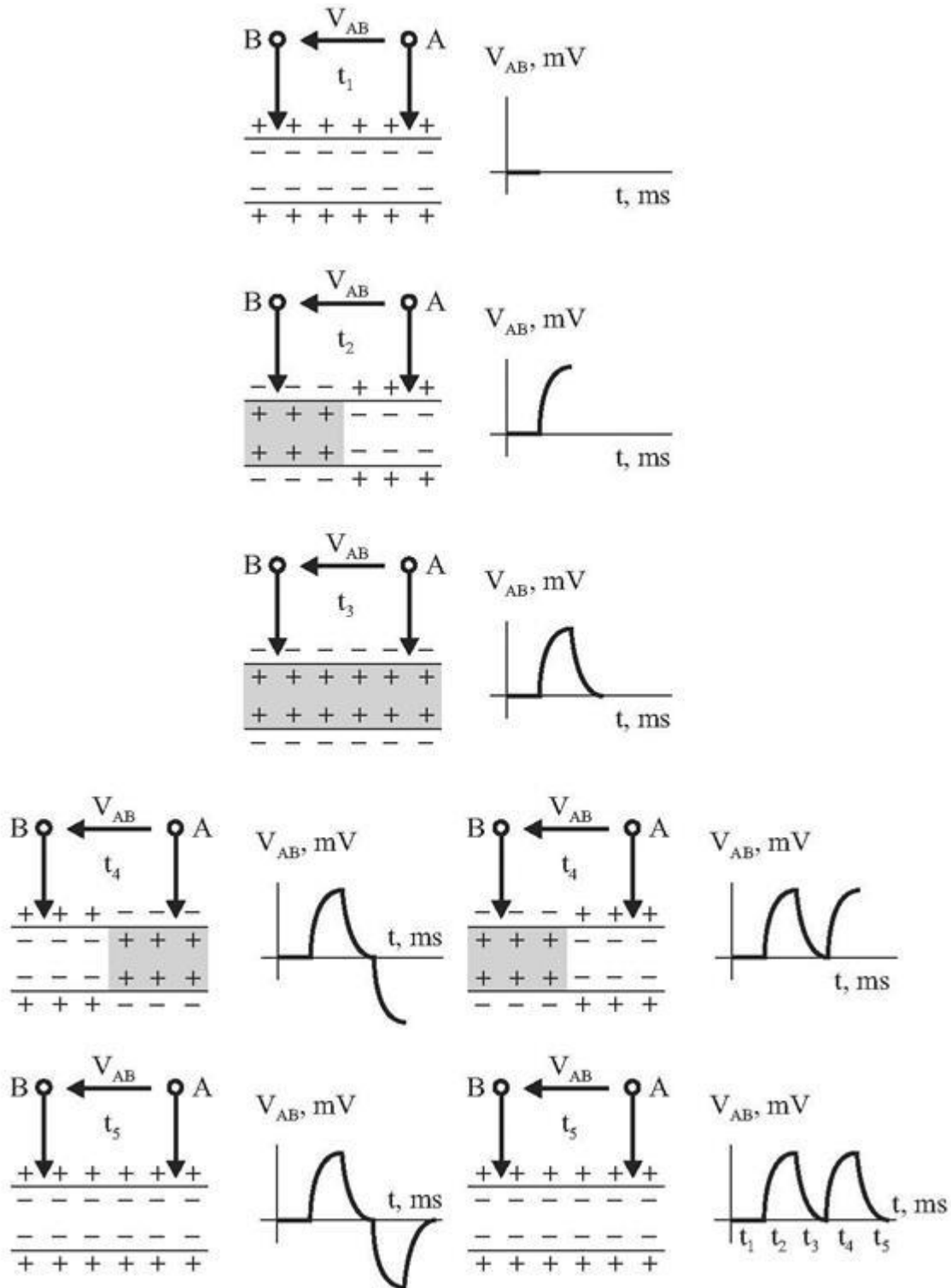


Figure 6.4 shows what we can measure during action potential when both electrodes are external to the cell but close to the membrane. The upper three subfigures show phases of a depolarization wave arriving from the left. At t_1 moment the whole cell membrane is polarized, at t_2 the wave reaches electrode B (but not A), at t_3 the membrane at both electrodes is depolarized. The lower subfigures to the left show the depolarization arrive also from the left. At t_4 repolarization has reached electrode B (but not A) at t_5 the whole membrane is in resting state again. The lower subfigures to the right show the repolarization arrive from the right. First electrode A is reached (t_4) and then the whole membrane is at rest (t_5). Animations illustrating the phenomenon:

http://project.mit.bme.hu/kobak2012/action_potential_propagation.pps

http://project.mit.bme.hu/kobak2012/action_potential_propagation_measured_externally.pps

Figure 6.4. Potential difference measured during action potential. Both electrodes are exterior of the cell.



2. Modelling the electrical activity of the heart

The electrical activity of the heart is monitored nearly always by measurement on the body surface. Consequently, *the resultant electrical activity of a great number of cells* is measured. An appropriate model is needed to estimate the electrical activity of the heart based on body surface measurement. The dipole model has been used since the late nineteenth century. The resting (polarized) and the active (depolarized) areas of the heart have different charge distribution. Observed from an external viewpoint, the active (depolarized) cell is negative compared to resting ones. Potential distribution can be modelled by a dipole on the boundary of active and resting parts (see Figure 6.5). The propagation of excitation means a resting-to-active change modelled by a

dipole moving along with its positive pole forward. Similarly, the active-to-resting change is modelled by a dipole moving along with its negative pole forward.

In 1889 – based on his measurements with electrodes on the body surface – Waller concluded the potential distribution at the moment of the contraction of ventricles (later named as R peak) given in Figure 6.6 [6.4]. The assumption is in agreement with body surface potential maps taken about a hundred years later.

Figure 6.5. Modelling with a dipole the boundary of resting and active parts

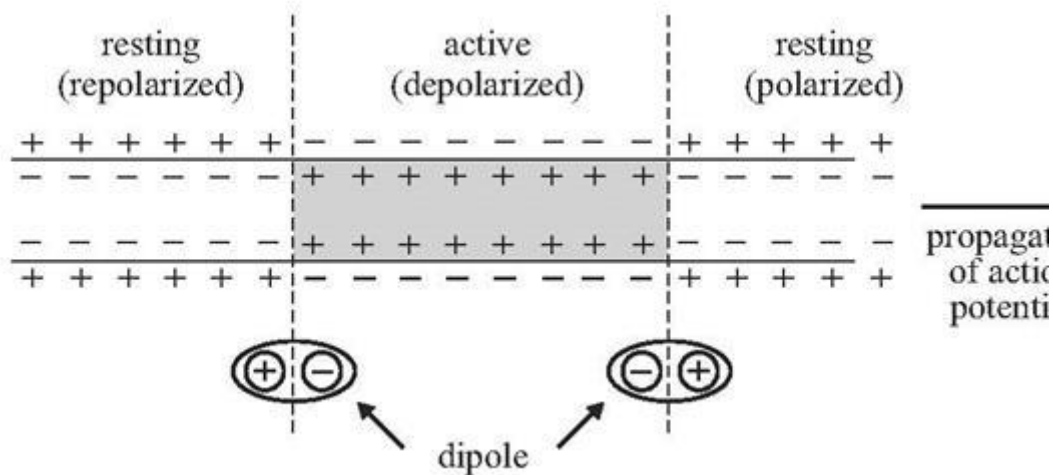
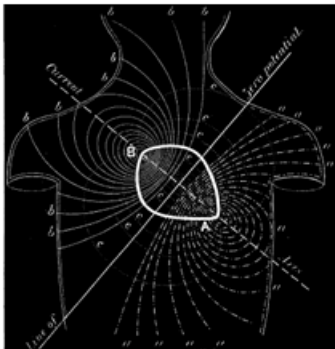


Figure 6.6. Waller's assumption on the body surface potential distribution at the moment of ventricular contraction <http://www.jstor.org/stable/91715?seq=18> (author: A. D. Waller, [6.4])



Nobel laureate Willem Einthoven established the basis of ECG evaluation. His suggestions have been widely accepted; these guarantee the standardized evaluation. Einthoven's hypotheses assume the following.

- I. The electrical activity of the heart can be depicted at every moment by a single dipole.
- II. Limb leads: the two shoulders and the left leg (originally the pubis) form an equilateral triangle; the heart is located at the centre of that triangle.
- III. Body fluids between the heart and the limbs have uniform resistance. These fluids determine the resistance between electrodes and the heart.

Einthoven's hypotheses and further widely used standard procedures assure that ECGs taken in different laboratories are equivalent.

In the frontal plane Einthoven's bipolar leads are used. The limb electrodes are: RA (right arm), LA (left arm), LL (left leg). The bipolar leads by definition:

$$\begin{aligned}
 I &= RA - LA \\
 II &= RA - LL \\
 III &= LA - LL
 \end{aligned}
 \tag{6.1}$$

The electrical activity of the heart can be analysed more effectively if three further leads are used in the frontal plane. These are unipolar leads, referenced to the central terminal (CT), also called Wilson point (see eq. 6.2).

$$CT = (RA + LA + LL)/3 \tag{6.2}$$

These unipolar leads originally were defined as the potential difference between the electrodes and CT, see eq. 6.3.

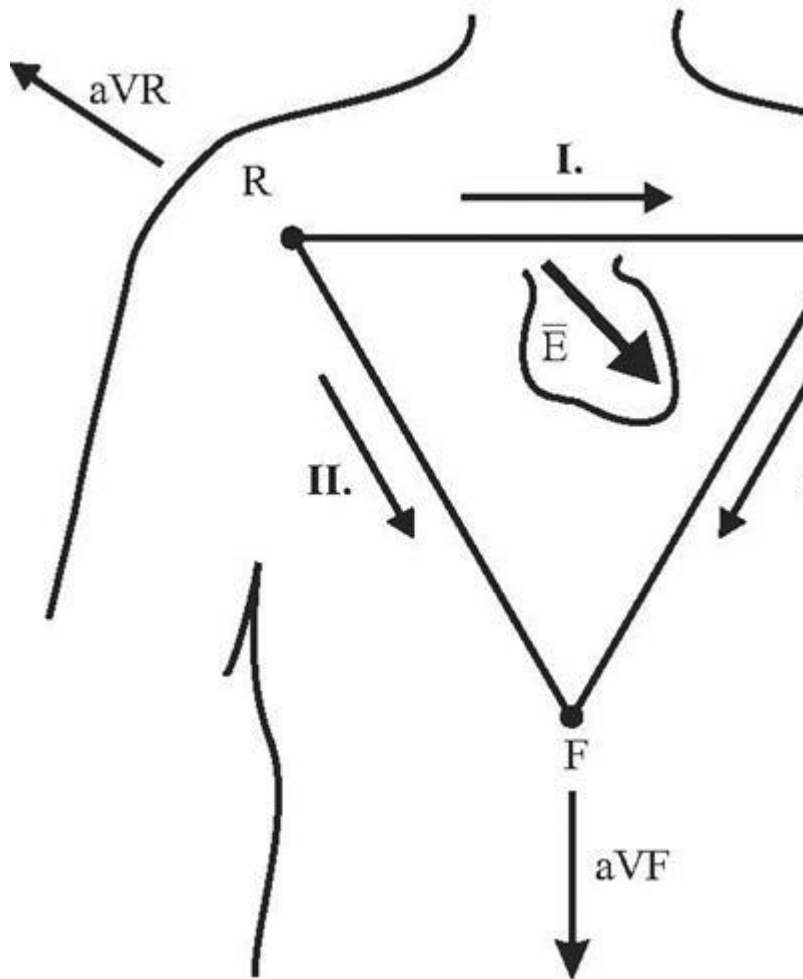
$$\begin{aligned}
 VR &= RA - CT = RA - (RA + LA + LL)/3 = (2RA - LA - LL)/3 \\
 VL &= LA - CT = LA - (RA + LA + LL)/3 = (2LA - RA - LL)/3 \\
 VF &= LL - CT = LL - (RA + LA + LL)/3 = (2LL - RA - LA)/3
 \end{aligned}
 \tag{6.3}$$

The amplitude of these leads can substantially be augmented (increased) by taking the difference of the potential between an electrode and the average of the other two. These leads are called augmented leads, see eq. 6.4.

$$\begin{aligned}
 aVR &= RA - (LA + LL)/2 = (2RA - LA - LL)/2 = 1.5 \cdot (RA - (LA + LL)/2) \\
 aVL &= LA - (RA + LL)/2 = (2LA - RA - LL)/2 = 1.5 \cdot (LA - (RA + LL)/2) \\
 aVF &= LL - (RA + LA)/2 = (2LL - RA - LA)/2 = 1.5 \cdot (LL - (RA + LA)/2)
 \end{aligned}
 \tag{6.4}$$

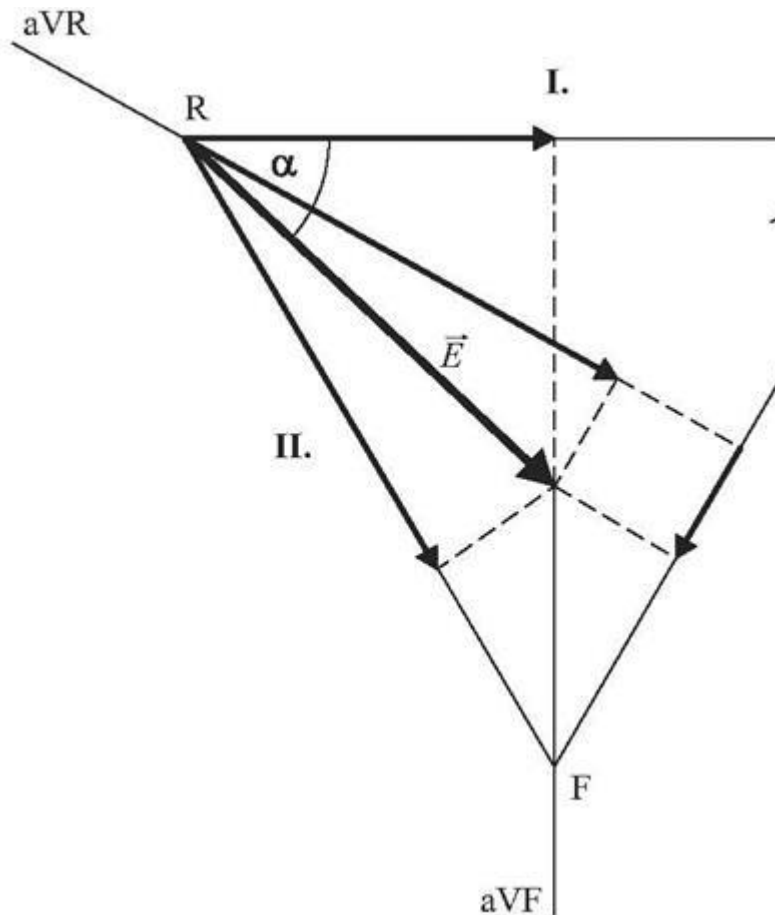
Figure 6.7 shows the relation between the electrical activity of the heart and the potentials in the frontal leads. The projection of the momentary resultant vector on the frontal plane is $\vec{E}$. The projections of $\vec{E}$ in the frontal leads are the following. In Figure 6.7 lead II is nearly parallel to $\vec{E}$ thus its projection to lead II has almost the same absolute value. The projection to lead I, III, aVL and aVF is in the same direction (positive) as $\vec{E}$ while the projection to lead aVR is negative. Momentary voltage value (represented by the absolute value of the projection) in lead I and aVF is 0.5 ... 0.7 times the absolute value of $\vec{E}$. $\vec{E}$ is nearly perpendicular to lead III and aVL. In these leads the momentary voltage value is 0.1 ... 0.2 times the absolute value of $\vec{E}$. The angle between lead aVR and $\vec{E}$ is nearly 180° . The voltage in lead aVR is negative; the absolute value is about the same as the absolute value of $\vec{E}$.

Figure 6.7. The Einthoven triangle and the frontal leads



It must be taken into account that aVR, aVL and aVF values, calculated according to eq. 6.4 are not equal to the projections of $\bar{E}$ to vector directions aVR, aVL and aVF! The difference comes from the difference between the length of the median and the side of Einthoven's equilateral triangle. The values resulting from eq. 6.4 must be multiplied by $1/\sin 60^\circ$ to get the correct projection values. Figure 6.8 illustrates this, where $\alpha = 45^\circ$. In the figure $\bar{E}$ is the projection of the resultant dipole to the frontal plane. The projection of $\bar{E}$ to direction lead aVR is equal to the projection to direction lead II, surely greater than $(I + II)/2$. Nevertheless, during ECG signal processing calculation according to definitions 6.4 is usual. In the cardiologists' practice this means about 15% underestimation of aVR, aVL and aVF amplitudes. Further consequence is the error during calculating the electrical axis of the heart. The electrical axis is usually calculated from two perpendicular leads (e.g. I and aVF).

Figure 6.8. Projections of the resultant frontal vector to leads I, II, III and aVR



In a given moment the projection of the resultant electrical activity to the frontal plane is $\vec{E}$, its angle to horizontal line is α . The projections of $\vec{E}$ (its absolute value is E) to leads I, II, III, aVR, aVL, aVF are given in eq. 6.5.

$$\begin{aligned} I &= E \cos \alpha \\ II &= E \cos(60^\circ - \alpha) \\ III &= E \sin(\alpha - 30^\circ) \end{aligned} \quad (6.5)$$

$$\begin{aligned} aVR &= E \cos(\alpha - 30^\circ) \\ aVL &= E \sin(60^\circ - \alpha) \\ aVF &= E \sin \alpha \end{aligned} \quad (6.6)$$

When $\alpha = 30^\circ$ then the projections of E are: $I = E * \sqrt{3}/2$, $II = E * \sqrt{3}/2$, $III = 0$, the projection sin leads aVR, aVL, aVF are given in Table 6.1.

Table 6.1.

Lead	The projection in the direction of the lead	Calculating according to 6.4
aVR	-E	$-E * \sqrt{3}/2$
aVL	$E/2$	$E * \sqrt{3}/4$
aVF	$E/2$	$E * \sqrt{3}/4$

Only two leads are independent of the six frontal leads (I, II, III, aVR, aVL, and aVF) applying Einthoven's hypotheses. When the values of any two leads are known, then the other four leads and the angle between the resultant frontal vector and the horizontal line can be calculated.

3. Measuring the electrical activity of the heart

Figure 6.9. Potential-time functions at different points in the heart and their summed resultant http://en.ecgpedia.org/wiki/File:Conduction_ap.svg

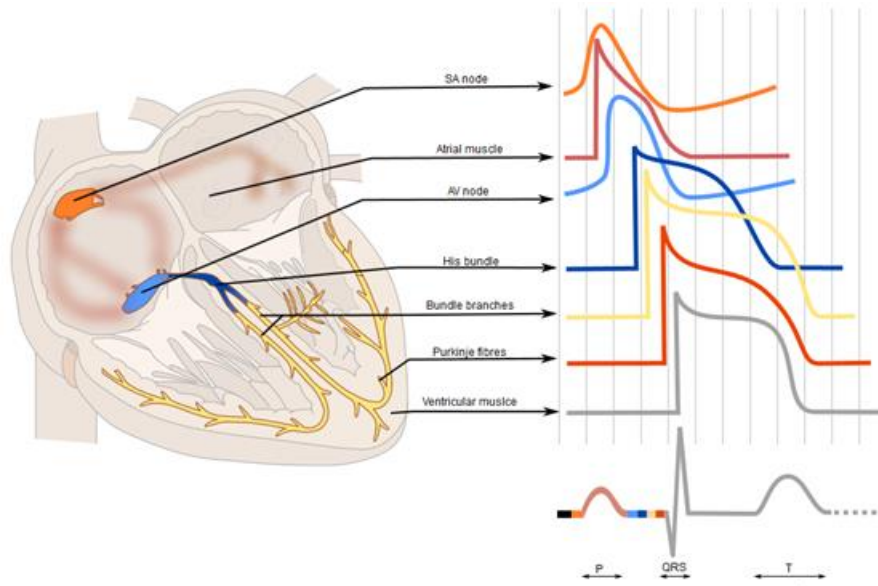


Figure 6.9 shows that at certain points along the nerves in the heart the potential-time functions contain action potentials with long refractory period. The typical wave shape depends on the location of the cell. The summation of the waveforms of all cells in the heart (bottom) is the well-known ECG waveform; this is present on the body surface. The figure illustrates that calculating the waveform at a given point from the resultant wave (solving the inverse problem) does not give an unequivocal answer.

The transfer function of the tissues and fluids between the heart and the electrodes is unknown. Inverse problem (see chapter 6.7) is to determine the electrical activity of the heart that could have caused the ECG signal measured on the body surface. The free simulation program (ECGSIM [6.5]) illustrates the electrical activity of the ventricles. The parameters of the action potential (amplitude and length) at a given point influence the signal shape in different leads. Changing the action potential at a given point can be seen well in certain leads while it may remain undetected in other leads. The inverse problem can be studied using the simulation program. Figure 6.10 shows the operator interface of ECGSIM.

Figure 6.10. The operator interface of the ECGSIM programme (van Oosterom A, Ostendorp T, [6.5])

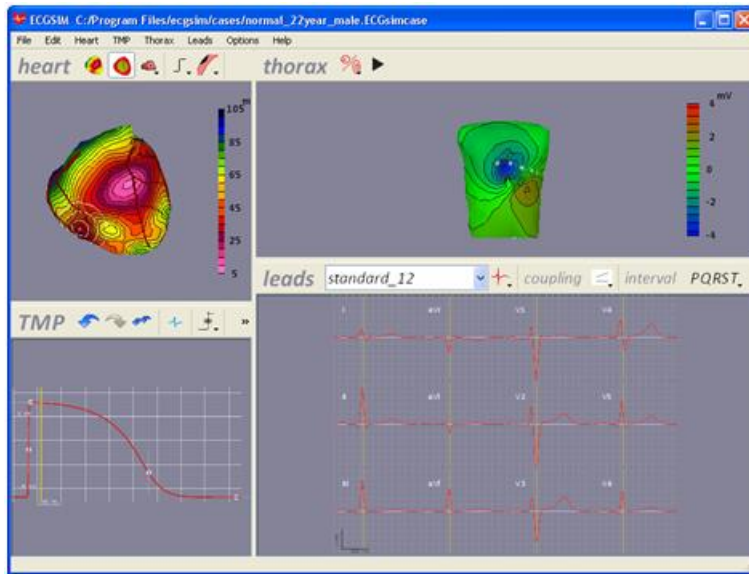


Figure 6.11. Orthogonal planes used for describing the electrical activity of the heart

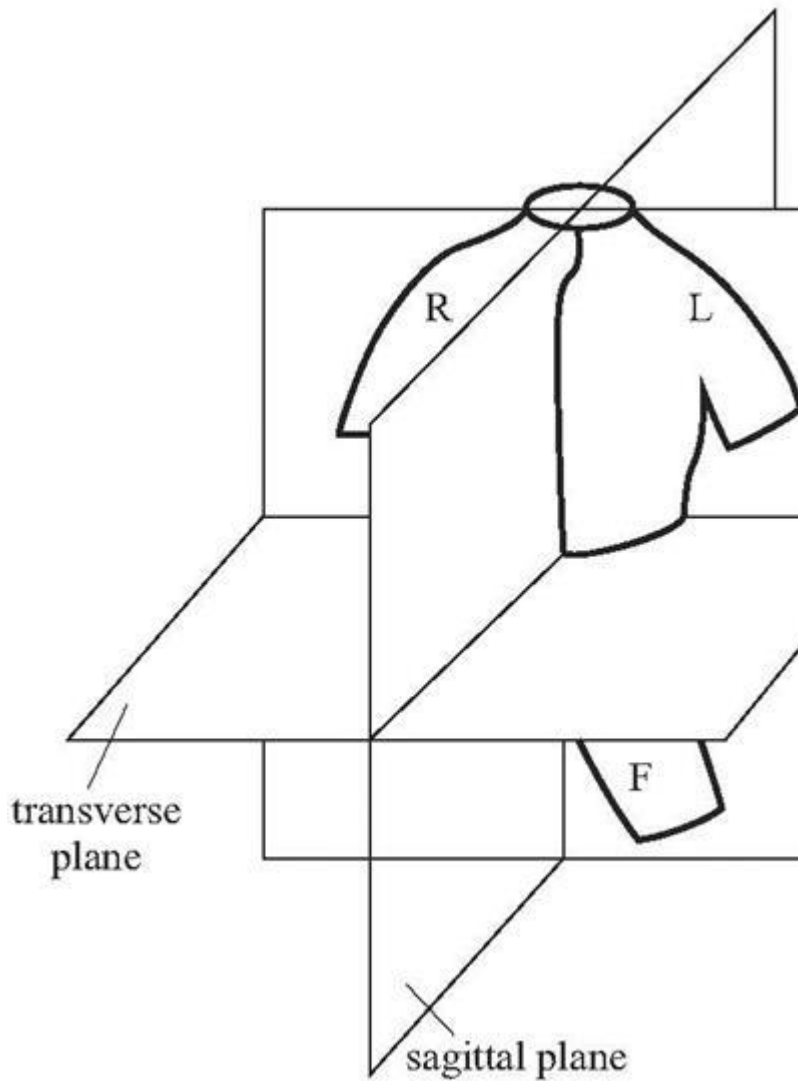


Figure 6.11 shows the three planes used to characterize the electrical activity of the heart. The projection on the transverse plane is measured with chest electrodes (their placement is given in Figure 6.12, the leads are called precordial). The projection on the sagittal plane is measured with the electrode in the oesophagus (see Figure 6.13).

Figure 6.12. Placement of chest electrodes that measure the electrical activity of the heart in the transverse plane (precordial leads)

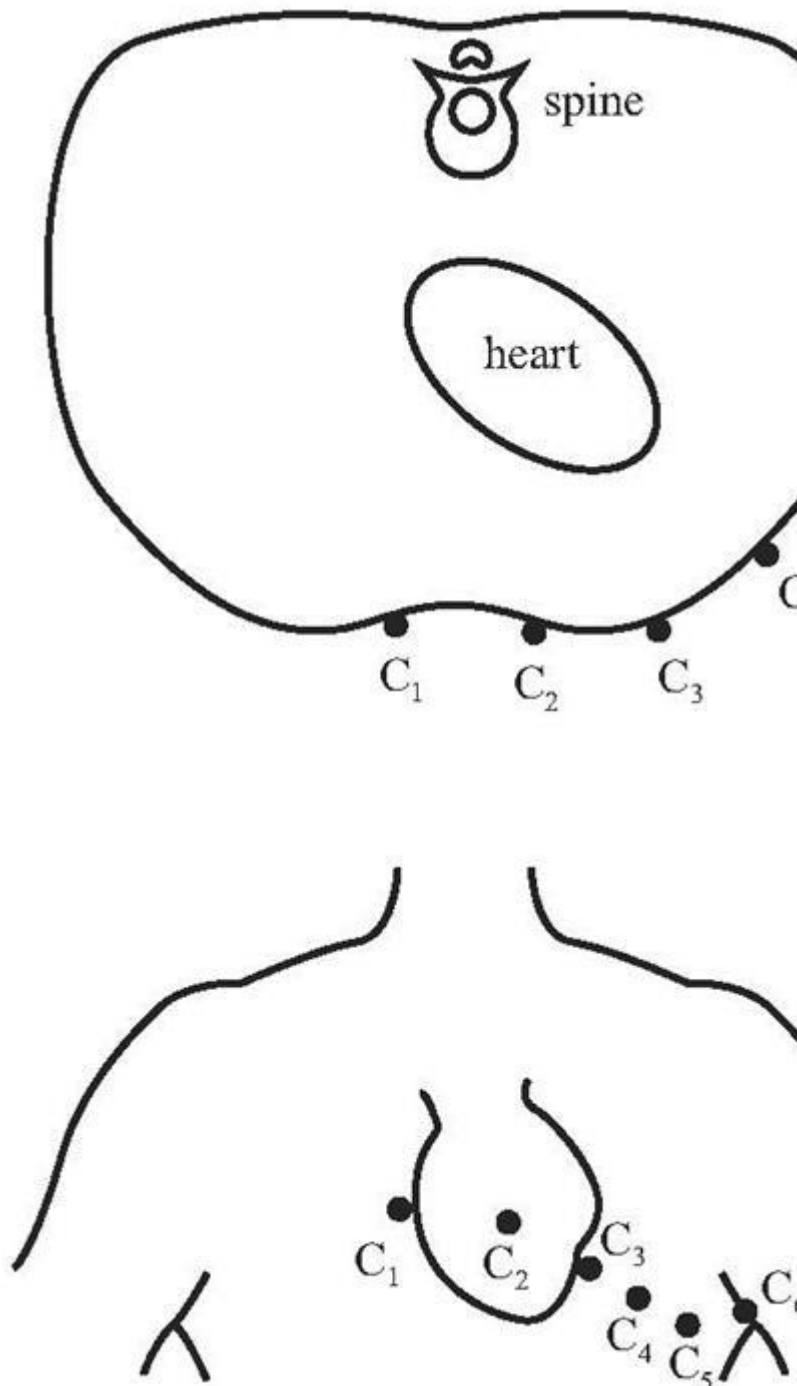


Figure 6.13. Placement of the electrode in the oesophagus to measure the electrical activity of the heart in the sagittal plane

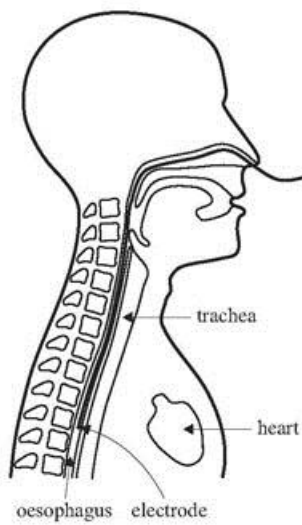
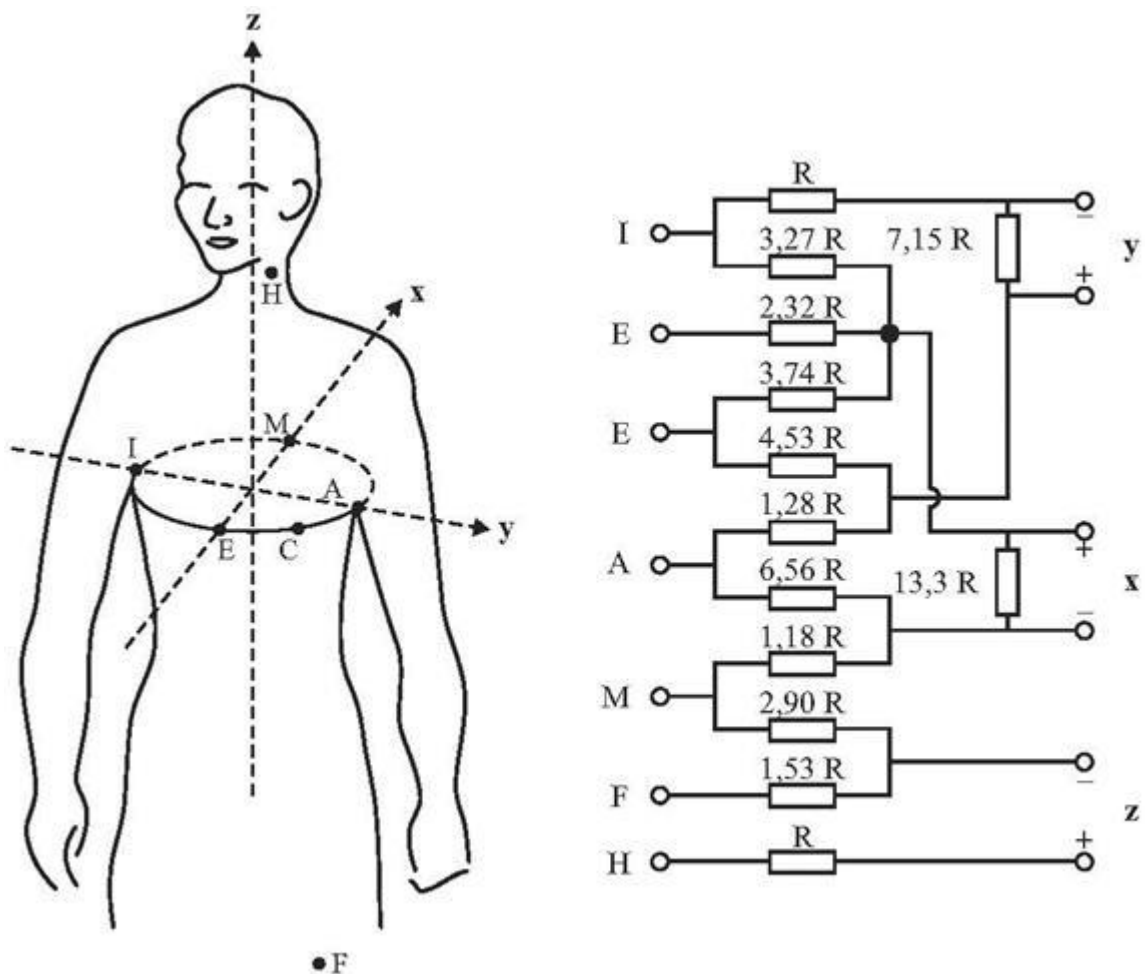


Figure 6.14. Electrode arrangement used for vectorcardiography (left). The Frank resistor network (right) generates the signals (x, y, z) necessary for three dimensional display



Recording signals in three orthogonal planes (see Figure 6.14) makes possible to display the electrical activity of the heart (concentrated in a dipole) in 3D. This is called vectorcardiography. Figure 6.15 shows the characteristic movement of the vector during a heart cycle (the reference point is in the origo).

Figure 6.15. Spatial vectorcardiogram and its projections to frontal, transverse and sagittal planes

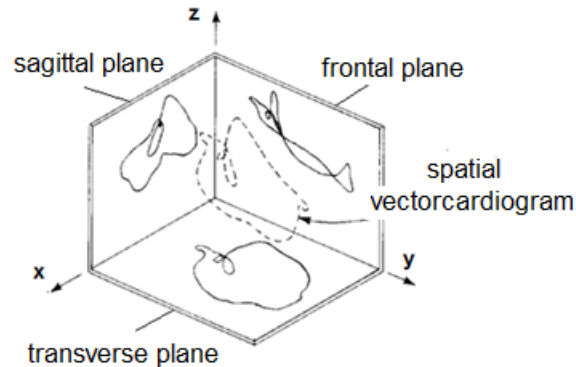
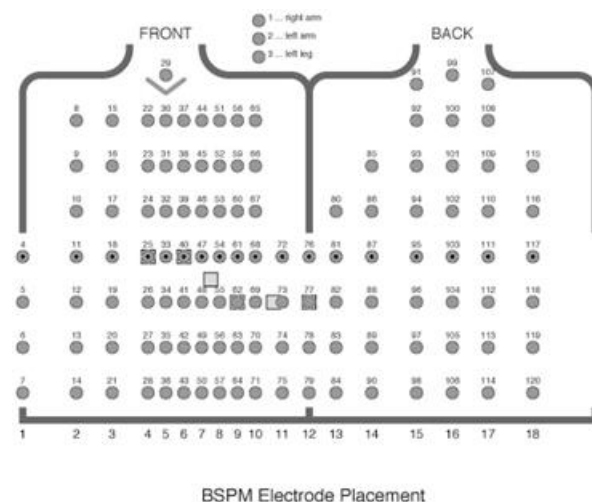


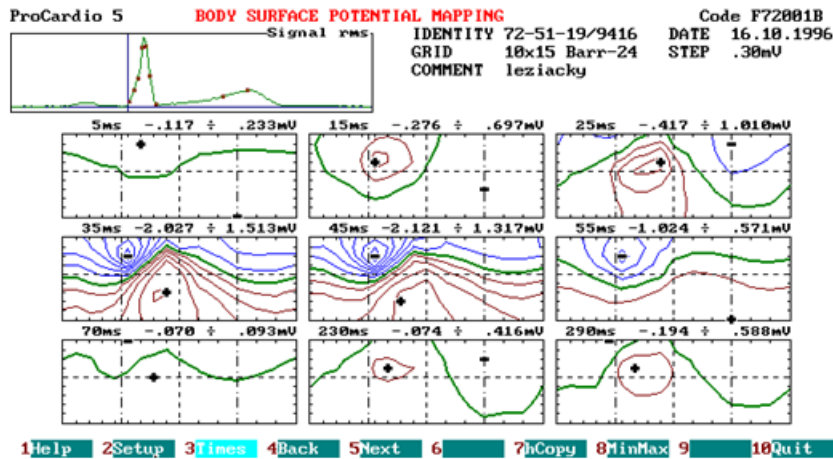
Figure 6.16. 120-electrode arrangement for body surface potential mapping
<http://www.sci.utah.edu/~macleod/bioen/be6000/labnotes/ecg/descrip.html> (authors: MacLeod R, Birchler B)



Body Surface Potential Mapping, BSPM [6.18], [6.20], [6.21] is also used to characterize the electrical activity of the heart. 32...200 electrodes are placed on the patient's body and the electrical activity of the heart is calculated on the basis of the measured voltage-time functions. Figure 6.16 shows a 120-electrode arrangement. Research laboratories apply different electrode arrangements. Conversion between these arrangements is very limited. BSPM is able to locate with cm accuracy the abnormal accessory electrical conduction pathway between the atria and the ventricles (Wolff-Parkinson-White syndrome). Figure 6.17 shows the changes in the body surface potential map of a patient for 285 ms [6.19].

Magnetoencephalography, MEG was first applied to test the brain's activity in the late 1960s. Measuring the biomagnetic activity of the heart (magnetocardiography, MCG) is technically simpler and easier. Nevertheless, even today such measurements are done only in research laboratories. Parallel ECG and MCG measurements can increase the diagnostic ability [6.6].

Figure 6.17. Illustration of the change of the body surface potential map during 285 ms
http://www.um.sav.sk/old/dep_5/maps_en.htm (author: Tysler M et al.)



4. Characteristics of the ECG time function

The ECG signal recorded in one heart cycle is normally composed of the following parts (Figure 6.18):

- P wave – atrial depolarization,
- PR interval – propagation of depolarization from the SA node to exit from the AV node,
- QRS wave – ventricular depolarization,
- ST interval – ventricles are depolarized,
- T wave – ventricular repolarization,
- TP interval – the whole heart is at rest.

Ventricular depolarization overlaps (and thus masks) the atrial repolarisation. If a U wave is present (normally it has very small amplitude or is completely absent) it follows the T wave its amplitude is in the same direction as the T wave. The origin of the U wave is not fully clarified.

Figure 6.18. Schematic ECG time function with the characteristic points



ECG signal is evaluated by medical doctors, most often by cardiologists. Evaluation is helped by calculating the following parameters:

Characterising the heart rate:

- momentary heart rate (frequency),
- heart rate (frequency) averaged over a few cycles,
- heart rate variability.

Time intervals within one heart cycle:

- PR interval, t_{PR} (from the beginning of P wave to the beginning of QRS complex),
- QT interval, t_{QT} (from the beginning of QRS to the end of T wave),
- QRS duration, t_{QRS} (from the beginning of Q wave to the end of S wave).

Limits of normal values (60/min heart rate):

- t_{PR} : 120 – 200 ms,

- t_{QT} : 350 – 430 ms,
- t_{QRS} : max. 120 ms.

t_{QT} is also influenced by the momentary heart rate. The corrected value (t_{QTc}) gives the estimation what would be the value if the heart rate was 60/min. The most frequently used correction is the Bazett formula, see eq. 6.6.

$$t_{QTc} = \frac{t_{QT}}{\sqrt{\frac{t_{RR}}{t_{RR}(\text{pulse rate}=60)}}} \quad (6.7)$$

where t_{QTc} is the corrected, t_{QT} is the actual value, t_{RR} is the length of the actual heart cycle (the time interval between two adjacent R peaks), $t_{RR}(\text{pulse rate}=60)$ is the value ($t_{RR} = 1$ s) when the heart rate is constant, 60/min.

Shape analysis within a heart cycle:

- the potential during the ST interval compared to the potential during the PR interval (also called ST elevation),
- shape and amplitude of the R peak, the area under the R wave,
- shape and amplitude of the P wave, the area under the P wave,
- shape and amplitude of the T wave, the area under the T wave.

Regarding the origin, each heart cycle can be 'normal' (depolarization emanates from the SA node), or 'extra'.

ECG recordings taken in the Einthoven I lead are available at the web page:

<http://www.mit.bme.hu/projects/bpmeas>

The videos below illustrate how the recordings were taken.

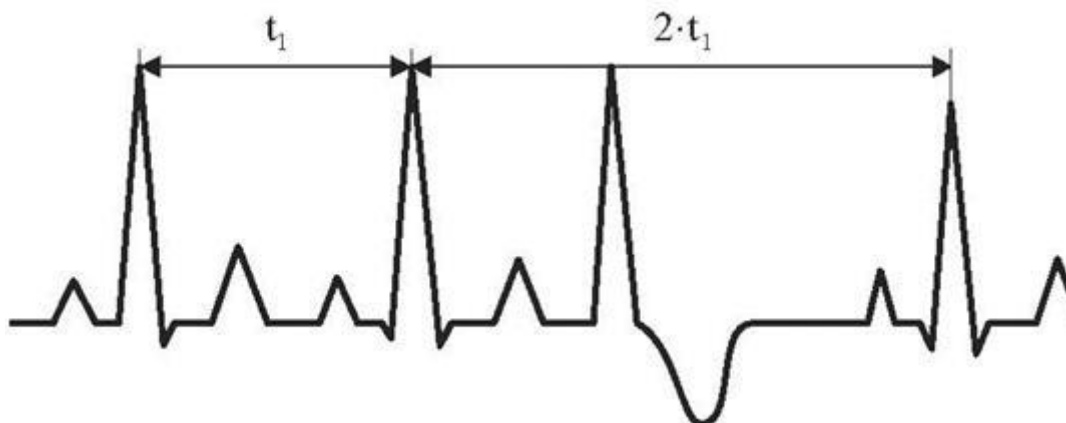
http://project.mit.bme.hu/kobak2012/ECG_PPG.wmv

http://project.mit.bme.hu/kobak2012/breathing_ECG.wmv.

5. Pathologic ECGs

Effective signal processing is helped if not only the normal but also the pathologic waveforms (most frequent distortions) are known. Premature cardiac contraction – independent of the normal rhythm – is triggered by a pulse arising outside the SA node. The source of the pulse can be in the wall of the heart or along the nerves the pulse from the SA node normally passes by. Such heart cycles are also called extrasystole. Figure 6.19 shows an example.

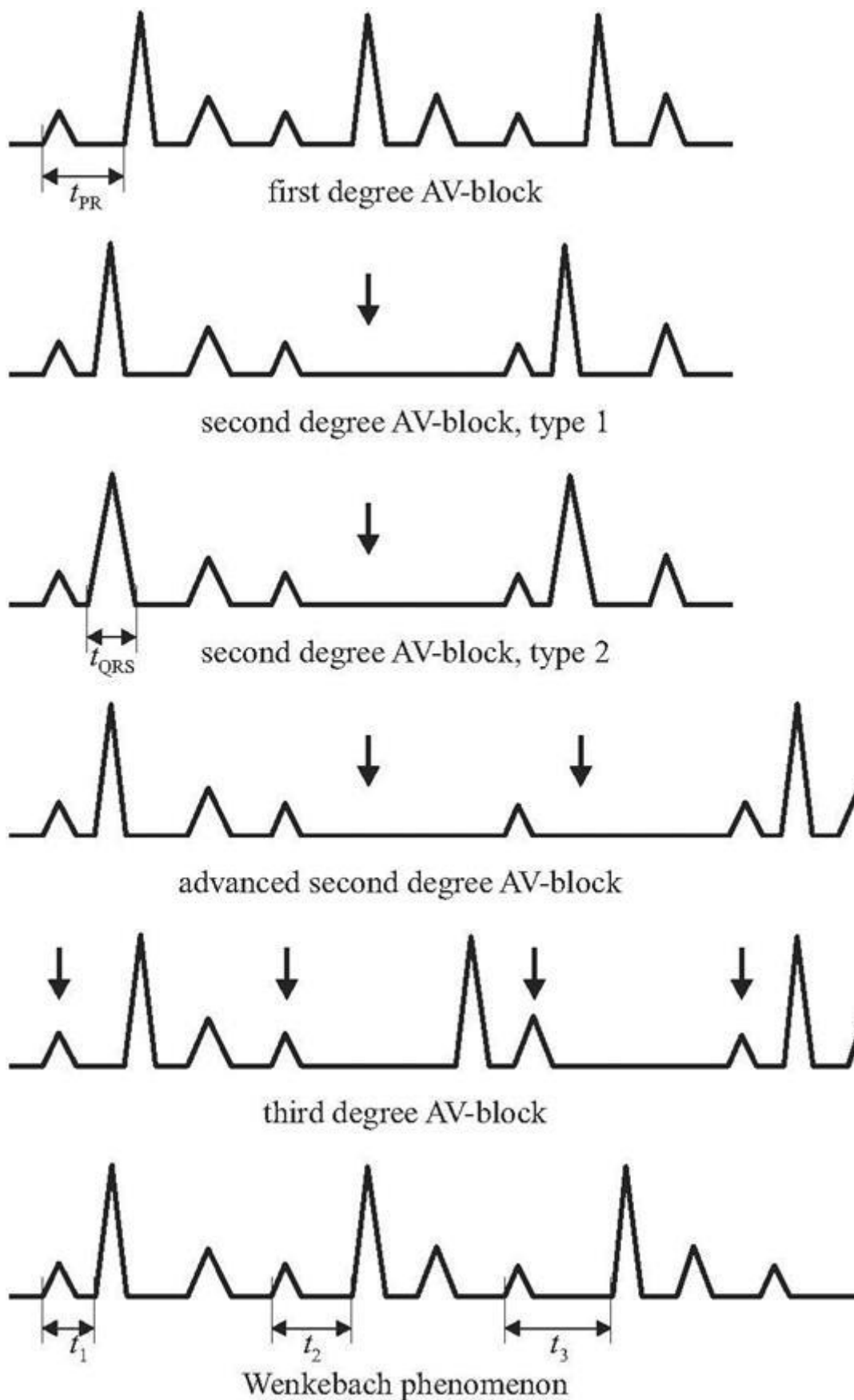
Figure 6.19. Premature ventricular beat, PVB



Arrhythmias can arise from the ventricles for various reasons. Diagnosing such cases requires the expertise of a cardiologist. The main categories are given in [6.7] and [6.8]. Most frequently the disorders of the pulse conduction system are related to the AV node. These conduction diseases are illustrated in Figure 6.20. The main categories are [6.7]:

- first degree AV-block,
- second degree AV-block, type I,
- second degree AV-block, type II,
- advanced second degree AV-block,
- third degree (complete) AV-block,
- Wenkebach phenomenon.

Figure 6.20. AV conduction diseases



First degree AV-block increases the PR interval, the increased value is constant. The reason of second degree type I AV block is intermittent conduction disorder. Atrial depolarizations occur normally and regularly and the

shape of QRS complexes is also normal. But not all atrial depolarization is followed by ventricular depolarization. In other words, not each P wave is followed by a QRS complex. In Figure 6.20 an arrow points to the place where the QRS complex is missing.

Second degree type II (also called Mobitz type II) AV block is caused by the disease of the conduction system distal from the AV node (in bundle of His, bundle branches or even in the Purkinje fibres). The result is the widening of the QRS complex to more than 100 ms. The PR interval (if QRS exists) is constant. Not all P waves are followed by a QRS complex. In Figure 6.20 an arrow points to the place where the QRS complex is missing.

In advanced second degree AV block two or more consecutive P waves are not followed by a QRS complex. The reason is the intermittent disturbance in the AV node. If a QRS complex exists then the preceding PR interval is constant. In Figure 6.20 arrows point to the places where QRS complexes are missing.

The third degree (or complete) AV block isolates the electrical activity of the atria from the ventricles. Atrial depolarization does not propagate to the ventricles. QRS complexes are independent of the P waves. Two independent rhythms are present in the ECG. Electrical activity in the ventricles is triggered by an accessory pacemaker in the ventricular wall. The resulting rhythm is called escape rhythm. Accessory (latent) pacemaker cells remain inactive while electrical pulse (depolarization) from the SA node arrives to them in time. In Figure 6.20 arrows point to the P waves. The T wave following the second QRS complex overlaps with a P wave.

The Wenkebach phenomenon is the progressive prolongation of conduction time in consecutive heart cycles. If the PR interval is involved then the lengthening will last until a QRS complex is skipped. PR interval drops to the normal value then starts lengthening again.

Myocardial infarction results from the interruption of blood supply to a part of the heart, causing heart cells to die. The dead area is unable to contract; its electrical state cannot be changed. The effect of the dead area changes in time in the ECG which makes diagnosing difficult. Figure 6.21 shows the hyperacute, acute and chronic phase of an infarction in lead V₃. The hyperacute phase starts a few minutes after the occlusion of the coronary artery and lasts for a few hours. In this phase the typical ECG speciality is the change in ST segment and T wave. The acute phase starts a few hours after the infarction and last for 3 ... 6 months. In this phase the negative Q wave, the ST elevation and the negative T wave are typical. In the chronic phase the negative Q wave, isoelectric ST segment and positive T wave are typical. Depending on the location and extension of the infarction various deviations can develop in the ECG [6.9].

Figure 6.21. The effect of myocardial infarction in the ECG in the hyperacute, acute and chronic phase in lead V₃



Fibrillation of the heart is life threatening [6.17]. Depolarization and repolarization are not coordinated. In case of ventricular fibrillation the heart stops pumping blood causing death in a few minutes. Figure 6.22 shows atrial while Figure 6.23 ventricular fibrillation.

Figure 6.22. Atrial fibrillation (top), normal heart rhythm (below)
http://commons.wikimedia.org/wiki/File:Afib_ecg.jpg (author: Heuser J)

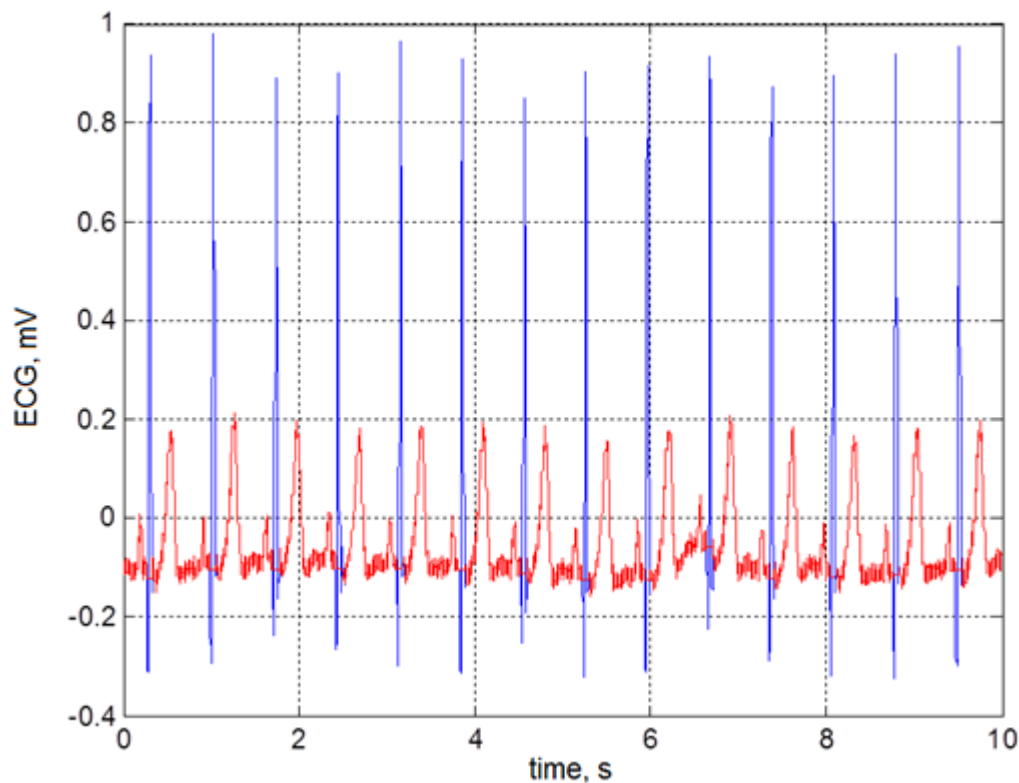


Figure 6.23. Ventricular fibrillation in different ECG leads
http://en.wikipedia.org/wiki/File:Ventricular_fibrillation.png (author: Roediger J)



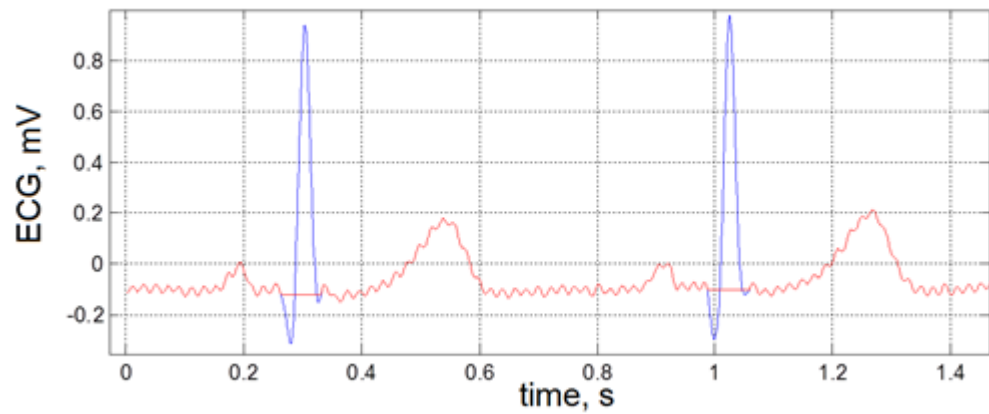
6. ECG signal processing

Figure 6.24. ECG recorded from a healthy senior male in Einthoven I lead (blue). The signal after removing the QRS complexes (red).



The QRS complex is a characteristic component of the ECG signal. The QRS has the steepest slope and usually the highest amplitude. QRS detection is typically the first step in ECG signal processing [6.10]. When the location of the QRS is known further segments of the ECG can be detected easier. Figure 6.24 shows a 10-s part of an ECG recorded in Einthoven I lead from a senior healthy male. The DC component has been removed (by subtracting the mean value of the record from each data) and a third order Butterworth low-pass filter (corner frequency 40 Hz) has been applied. The filtered ECG is in blue, and the signal after QRS complexes have been removed is in red.

Figure 6.25. Two cycles from the signal shown in Figure 6.24, the original signal (blue) and the one after QRS complexes have been cut off (red)



Two cycles are enlarged in Figure 6.25. The filtered signal is in blue, the signal after QRS complexes have been cut off is in red. Figure 6.26 shows the frequency spectrum of the two signals. The removal of the QRS complexes makes a difference in the 8 – 35 Hz range.

Figure 6.26. Frequency spectrum of signals shown in Figure 6.24

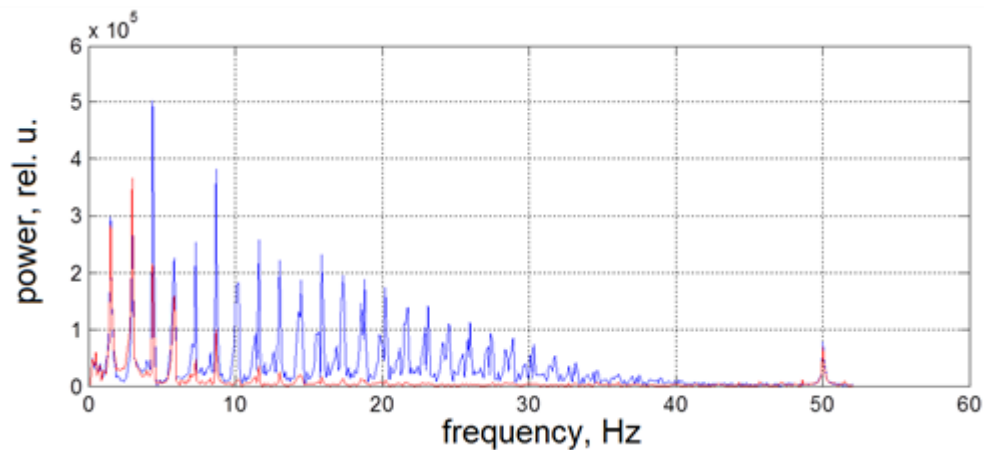


Figure 6.27 shows the frequency spectrum of the recorded ECG (blue) and the signal after the T waves have been cut off. Figure 6.28 shows the 0 – 10 Hz range. The removal of the T waves makes a difference in the 3 – 6 Hz range.

Figure 6.27. The frequency spectrum of the signal shown in Figure 6.24 (blue) and of the signal after T waves have been cut off (black)

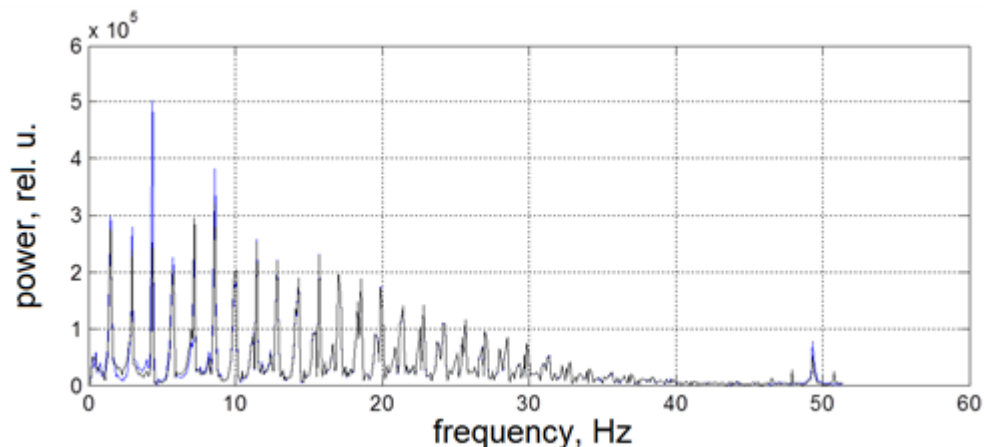
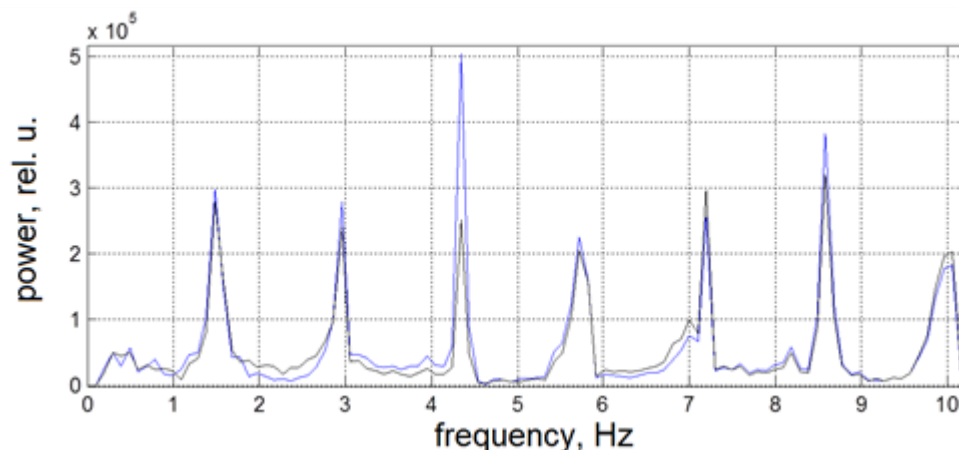


Figure 6.28. The 0 – 10 Hz enlarged from the spectrum in Figure 6.27

Bandpass filtering (most common range 10 ... 20 Hz) is advantageous in QRS detection. The quality factor (Q) of the filter is usually around 1. Greater Q would result in oscillations in the transient response. The high steepness of the QRS complex explains the use of differentiation. This separates QRS complexes from P and T waves. Differentiation is equivalent to high-pass filtering, thus power line noise and EMG signals can also be enhanced. This effect is compensated by calculating the effective value of the signal over a given interval. The interval is equal to the normal width of QRS (60 – 100 ms). The QRS complexes are determined by thresholding the effective value – time function. The above described method is the Pan – Tompkins QRS detector [6.11] which will be detailed in section 4.2.1.

Pattern matching is also applied for QRS detection. The pattern can be generated from the ECG recorded from the patient. This fits to 24-h (Holter) monitoring: the QRS pattern is determined based on a 5 – 10 minute long recording while the patient is at rest. Neural networks can be applied for QRS detection with pattern matching [6.24].

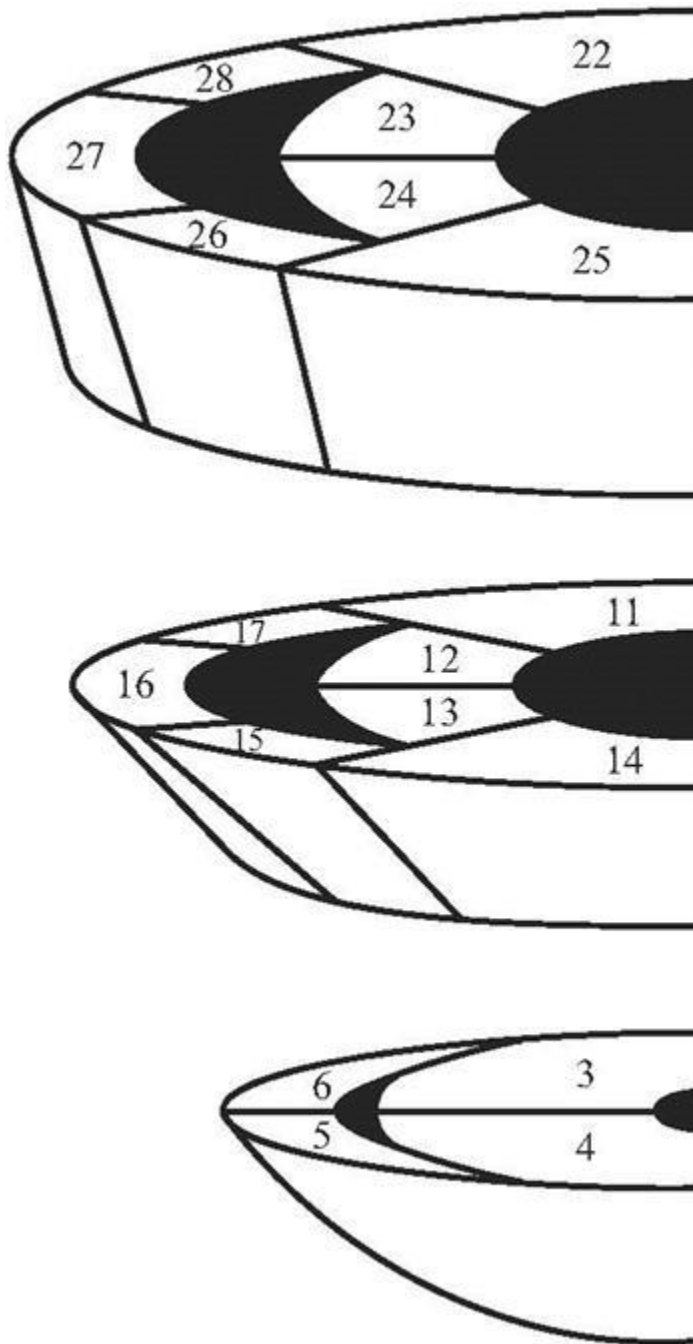
Removal of baseline wander and suppression of power line noise are also important in ECG signal processing. Baseline wander originates from breathing and the change of the half-cell potential at the skin-electrode interface. According to the standard an ECG equipment has a lower corner frequency 0.05 Hz (-3 dB). This reduces baseline wander but does not eliminate it. Increasing the lower corner frequency would further reduce baseline wander but would also distort P and T waves that have low frequency components. There are two methods to cancel low frequency noise. One is to identify the isopotential segments of ECG (e.g. PQ), fit a curve to these points and then subtract the curve from the signal. The other method is morphological filtering [6.12]. This hardly changes the relative positions of data points along a given pre-defined segment. Specifying the segment longer than the P and T waves these components remain unaffected while the longer low frequency baseline wander is suppressed. Power line noise filtering is aided by the fact that its frequency rarely deviates from the nominal (in Europe 50 Hz) by more than 0.1 Hz. Up-to-date ECG equipment apply digital filtering for power line noise suppression.

The frequency range of EMG noise is typically above 30 – 35 Hz. Its low frequency components overlap with the ECG signal; cannot be filtered in the frequency domain. Nevertheless, in ECG equipment in an intensive care unit or 24-h monitoring low-pass filtering with a 30 – 35 Hz corner frequency is typical to reduce EMG noise. In case of patients at rest EMG noise is negligible.

In the developed countries more and more people live with a pacemaker. The pacemaker gives a pulse with relatively high amplitude that can saturate the ECG amplifier. As the pacemaker pulse is short (a few ms) filtering is effective by limiting the maximum slope of the signal.

Recording of ECG signals is relatively simple; a great number of ECG recordings must be evaluated. In the mid-1980s the number of ECG recordings was estimated 200 million/year, half of which were evaluated by computer. Practically all present day ECGs apply a processor and evaluate the recorded signal by digital signal processing. Artificial intelligence, time-frequency analysis as well as conventional signal processing can be found in ECG equipment.

Figure 6.29. Finite element model (28 elements) of the heart



Recordings made by body surface potential mapping (BSPM) are often processed using finite element models. The method estimates how an element influences the time functions recorded on the body surface. Figure 6.29 shows a simple model for analysing the electrical activity of ventricles [6.19]. Models are available with several hundred, even with a few thousand elements [6.13].

Even with the effective computational background available today compression of ECG recordings may be necessary. Long recordings frequently for home health monitoring or remote availability of data can justify compression. Different methods are available: DWT, Discrete Wavelet Transform, FFT, Fast Fourier Transform, DCT, and Discrete Cosine Transform [6.14]. The slope of the ECG signal is small except for the QRS. This can be made use of while applying variable length coding. The difference of neighbouring points result in small values, short codes should be assigned to these frequent values.

7. Qualifying ECG processing algorithms

Diagnosis is made by deducing the state of the heart from the potentials measured on the body surface. The signals measured on the body surface could be caused by different heart activities. This is called inverse problem, see Figure 6.30.

Figure 6.30. Inverse problem: the electrical activity of the heart is estimated on the basis of potentials measured on the body surface, not knowing the exact parameters of tissues and body fluids (authors: Malmivuo J, Plonsey R [6.26])
http://www.elin.ttu.ee/mesel/Study/Courses/3240BME/Content/1_Bioelectricity/BME_2_bioelectric_signals.htm

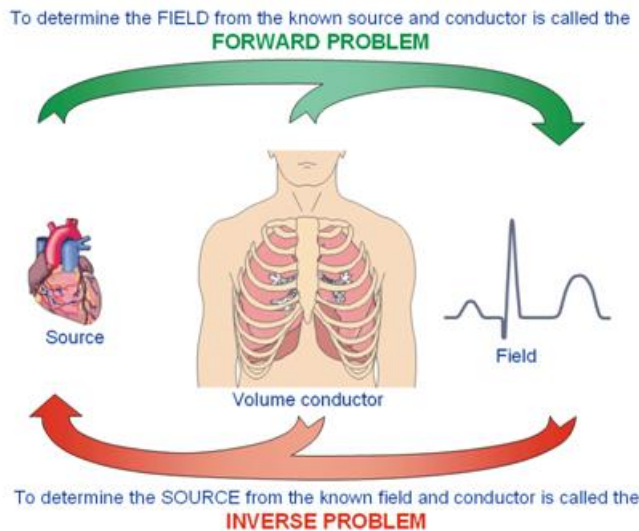
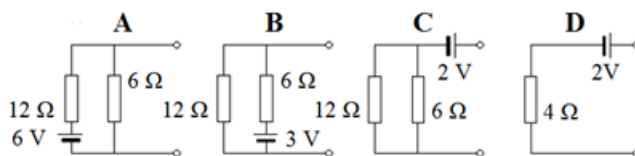


Figure 6.31 shows four possible circuits that have $4\ \Omega$ output resistance and $2\ \text{V}$ no-load output voltage. If only these two parameters are known then the elements of the circuit cannot be determined. But if further information is available then the circuit can be better specified. As an example, if we know that the circuit comprises a single voltage source and one series resistor, then its structure is the one shown in subfigure D (the two elements can be commuted).

Figure 6.31. There is no single solution to the inverse problem



Making the diagnosis based on the ECG is not the engineer's task. Engineers together with medical doctors work out the appropriate signal processing algorithms to increase signal-to-noise ratio and to determine the parameters characterising the ECG. The ECG signal processing methods are evaluated by using standard databases. These databases contain recordings that have been qualified (annotated) by cardiologists, thus the reference is included for calculating the sensitivity and specificity (positive predictivity). Both representative and rarely observed but clinically significant signals are in the databases.

The most popular standard databases [6.22] are:

MIT DB: The Massachusetts Institute of Technology-Beth Israel Hospital Arrhythmia Database (48 records, 30 minutes each).

AHA DB: The American Heart Association Database for Evaluation of Ventricular Arrhythmia Detectors (80 records, 35 minutes each).

ESC DB: The European Society of Cardiology ST-T Database (90 records, two hours each).

NST DB: The Noise Stress Test Database (12 records, 30 minutes each).

CU DB: The Creighton University Sustained Ventricular Arrhythmia Database (35 records, 8 minutes each).

The MIT-BIH arrhythmia database [6.16], [6.23] contains 30-minute long two channel ambulatory ECGs sampled at 360/s. Recordings were taken using chest electrodes. In nearly all records one channel is a modified Einthoven II lead, the other is a modified V1. Figure 6.32 shows a part of a record. All QRS complex is annotated. Annotation was done by at least two cardiologists independently of each other. The 110 000 QRS annotations have proved to be correct: during the past thirty years only one annotation had to be modified.

Figure 6.32. Figure 6.32. Nine annotated QRS complexes from a record in the MIT-BIH database <http://www.physionet.org/physiobank/database/mitdb/> (authors: Goldberger et al. [6.23], Moody GB et al. [6.16])



ECG signal processing algorithms tend to be optimal for the database used for its evaluation. The algorithms may perform worse for real-world records.

It is important to note that *change* in ECG signal of a patient is informative for the diagnosis. It follows that it is worth recording ECGs regularly, rarely for the young, and yearly for the elderly even if they have no heart problem. At present the easy (and automatic) comparison of such recordings is not solved.

The diagnosis suggested by automatic evaluation of the ECG must always be checked by the cardiologist. The advantage of automatic evaluation of the ECG is that never gets tired and always considers even rare diseases.

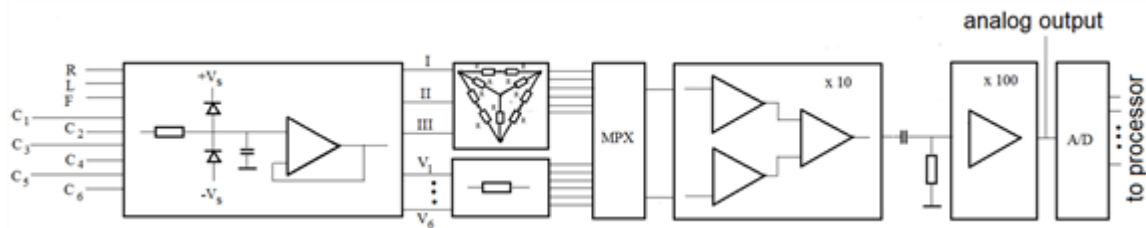
8. ECG equipment

There are different ECG device categories. Their field of application is different so they have to comply with different requirements. The major device categories are:

- diagnostic ECG to record signals at rest,
- stress (exercise) ECG,
- Holter (24-hour, ambulatory) ECG,
- ECG module in an intensive care patient monitor,
- ECG module in a cardioverter (defibrillator),
- telemetry ECG,
- foetal ECG.

Figure 6.33 shows a general block diagram for ECG equipment.

Figure 6.33. Functional scheme of one channel of a typical ECG equipment



The input circuitry in direct contact with the electrodes must have high input impedance. The minimal allowed input impedance can be calculated from the related standard [6.25]: it is $2.5 \text{ M}\Omega$. The voltage follower in the input stage assures this. The circuitry must be protected against input overvoltage. This can be realized by a series resistor and two diodes. The series resistor (together with the skin-electrode resistance) with a capacitor to internal ground forms a low-pass filter. The voltage followers (with small output resistance) drive the resistance network creating the voltages in different leads (see Figure 6.34). The actual lead can be selected with multiplexers of the outputs of the resistor network. The selected lead is connected to the input of an instrumentation amplifier (see chapter 3.4.1). If more than one lead has to be recorded in parallel each channel requires a separate multiplexer and instrumentation amplifier. The input stage generates the potential for body potential driving (DRL, driven right leg) increasing CMRR. According to the related standard the device must process ECG signals correctly even if a $\pm 300 \text{ mV DC}$ is added. Consequently the symmetrical amplification of the instrumentation amplifier cannot be higher than 10. The instrumentation amplifier is coupled to the main amplifier (usual gain is $50 \dots 100$) with an RC network that assures the low corner frequency ($0.05 \text{ Hz}/-3 \text{ dB}$). The total amplification is between 500 and 1000. The amplification of the device is called $\times 1$, if 1 mV symmetrical voltage produces 10 mm deflection on the paper.

In devices using the driven right leg technique the skin-electrode impedance can be continuously monitored. The output voltage of a square wave generator is added to the input of the DRL amplifier (see Figure 6.35). The square wave is a common signal; it will be present in each input connected to electrodes. Resulting from the big CMR the square wave at the input of the amplifier is negligible compared to the symmetrical input signal until the skin – electrode impedance is low. When an electrode falls of the square wave disappears in the related input; while its amplitude increases in the other inputs. This can be easily detected and the operator can be warned.

Figure 6.34. The (Wilson) resistor network that produces the frontal leads from limb electrode potentials

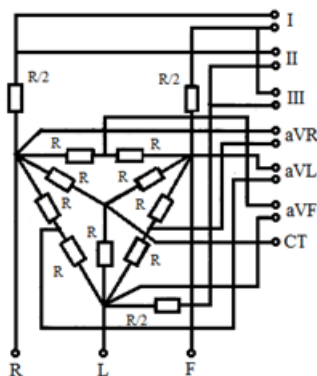


Figure 6.35. Continuous monitoring of electrode contact in an ECG device

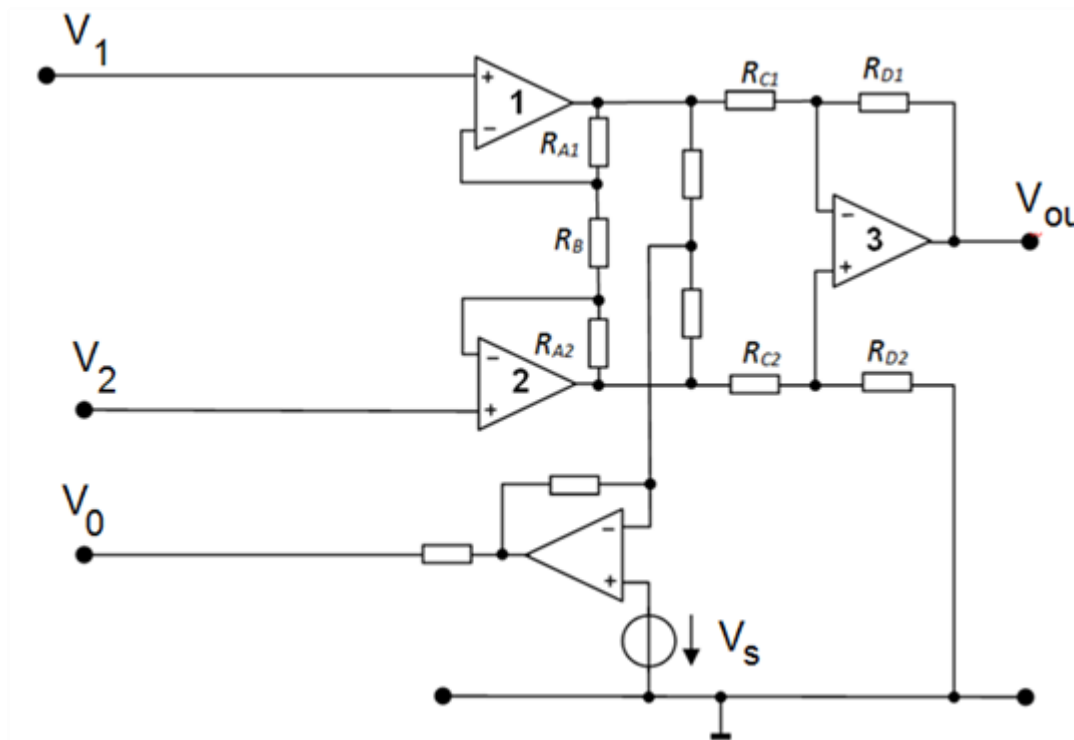
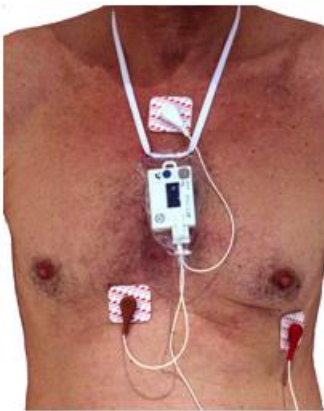


Figure 6.36. Disposable electrodes placed on the chest of a patient and a miniature Holter ECG for two-channel 24 hour recording (<http://commons.wikimedia.org/wiki/File:HolterAFT1000.jpg>, author: Faisandier)



Some heart abnormalities appear only intermittently. 24-hour (Holter) monitoring can reveal such abnormalities. Figure 6.36 shows a Holter ECG and three disposable electrodes on the patient's chest. The discomfort is minimal caused by 24-hour monitoring. Early Holter monitors recorded ECG on magnetic tape. The method had several difficulties: power supply, ultra thin thus stretching tape, very slow tape speed during recording, even high-speed playback lasted for hours. Modern devices use semiconductor memory, usually evaluate ECG on-line real-time. When an abnormality is detected the preceding and following some minutes are stored, using a buffer memory.

Figure 6.37 shows a printout of a 12-lead ECG. Usually three leads are printed in parallel: I-II-III, aVR-aVL-aVF, V1-V2-V3, V4-V5-V6. In Figure 6.37 the trace of lead II – as a reference signal – is always on the bottom. At the end of the printout the amplitude of the square wave corresponds to 1 mV.

Figure 6.37. 12-lead ECG printout on standard paper (http://commons.wikimedia.org/wiki/File:ECG_001.jpg author: Larson G)

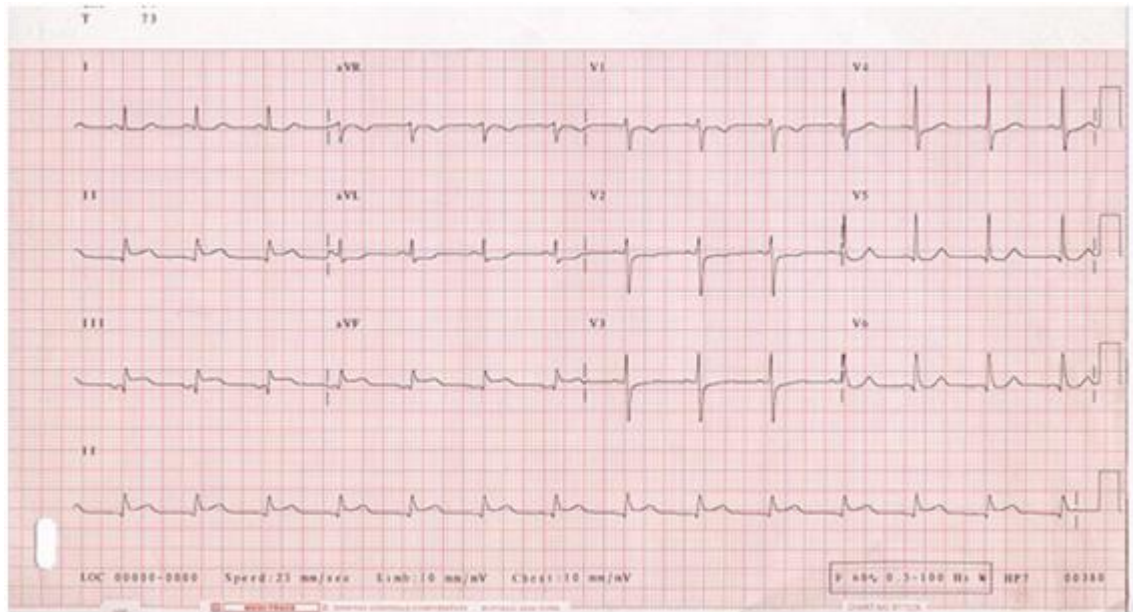


Figure 6.38 shows the standard ECG paper zoomed in. The normal paper speed is 25 mm/s. With this speed the width of a single small square represents 40 ms, the width of a large square (square with bold lines, covering 25 small squares) represents 200 ms. The gain referred to as „x1” will result in 10 mm displacement when the input (symmetrical) voltage is 1 mV. In other words, the height of a small square represents 0.1 mV. The standard grid helps the visual evaluation. It is easy to determine the momentary heart rate. If the distance between two adjacent R peaks is 4 large squares (800 ms) then the heart rate is 75/min. Up-to-date ECG equipment evaluate the recording and print the result on normal paper (standard grid is usually added).

Figure 6.38. ECG paper with standard raster

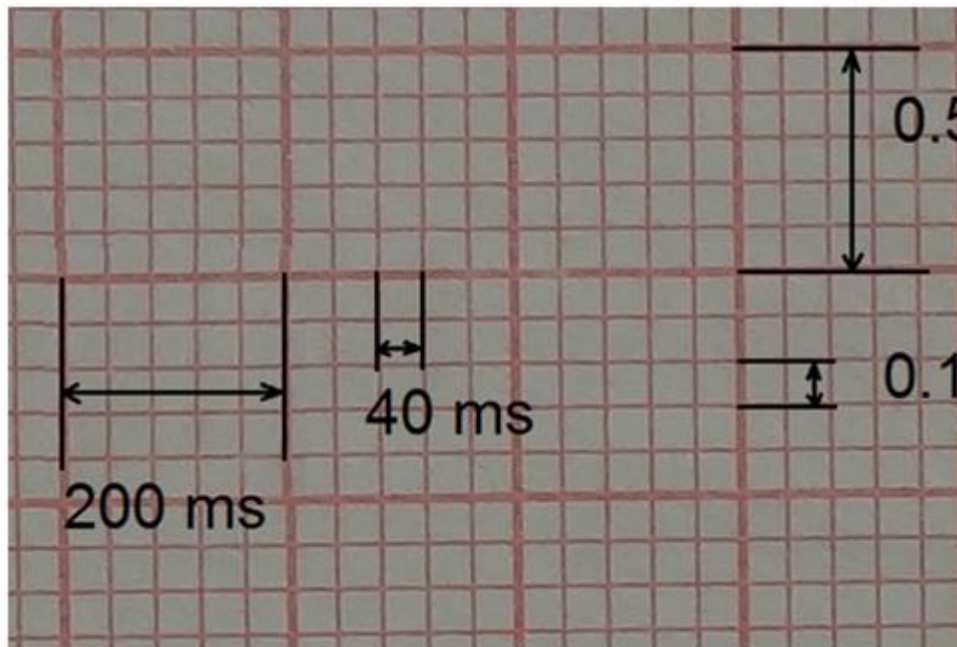


Figure 6.39 shows early ECG equipment. A state-of-the-art wireless ECG monitor is shown in Figure 6.40.

The transfer function of a DC decoupling circuit is equal to a high pass filter. Using high resolution AD converters (which are cheap enough to be incorporated into ECG equipment) the DC decoupling can be eliminated. This is advantageous for the distortion free transfer of P and T waves. The output of a usual input amplifier (see section 3.4) is directly connected to a high resolution AD. If ± 300 mV DC is added to the symmetrical input signal (peak-to-peak 1 mV) then in the worst case 10 bits are lost. If the resolution of the AD

is 24 bits then it is still possible to record the ECG signal with 12-bit resolution. This is enough for most of the applications. Cheap sigma delta converters are available with an equivalent sampling frequency of 1000 samples/s.

Figure 6.39. ECG equipment manufactured in 1911 by Cambridge Scientific Instrument Company
(http://commons.wikimedia.org/wiki/File:Willem_Einthoven_ECG.jpg Contrary to the filename the device was not made by Willem Einthoven.)

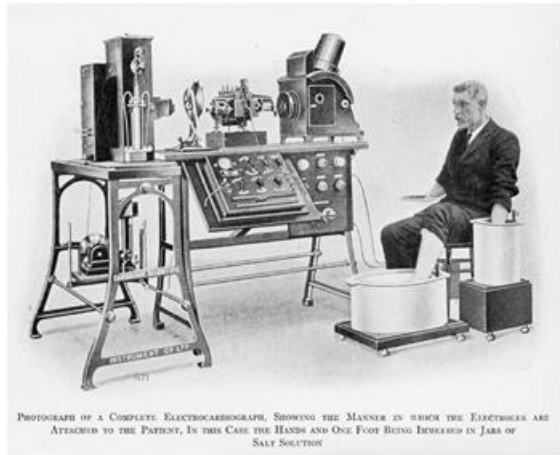


Figure 6.40. Figure 6.40. Wireless ECG monitor
(http://commons.wikimedia.org/wiki/File:Wireless_ECG_Monitor.jpg author: ?つぱー)



Integrated circuit is available which needs only a few additional components to be used as ECG equipment. TI ADS1298 comprises 8 programmable gain amplifiers, 24-bit resolution AD converters, the resistor network producing the Wilson potential, the driven right leg amplifier and the circuitry needed to detect the fall out of an electrode.

9. Problems

1. The R peak in the Einthoven I lead is 0.8 mV, in the aVR lead is -0.924 mV. Calculate the projection of the resultant dipole vector to the frontal plane and the angle between it and the horizontal line.
2. The DC decoupling circuit elements (Figure 6.33) are: capacitor 1 μ F, resistor 4.7 M Ω . Calculate the low corner frequency and the suppression of the circuit at 0.1 Hz.
3. At the input the peak-to-peak value of the
 - ECG signal is 1 mV,
 - power line (50 Hz) noise is 1V.

Calculate the signal-to-noise value at the output provided the resultant CMRR of the equipment is 100 dB. Calculate the necessary minimum resultant CMRR so that at the output the power line noise amplitude be less than 1% of the ECG signal amplitude.

4. The sampling rate of the ECG equipment is 1000 samples/s. Give the resolution of the momentary heart rate calculation.
5. What is the relation between the refractory period of heart cells and the maximum heart rate?
6. Based on a 100-s ECG record what frequency resolution is available?
7. The generator V_s in Figure 6.35 produces 1 Hz square wave. Draw the signal shape at the output of op amp 1 and 2 provided the skin-electrode contacts are perfect.
8. The generator V_s in Figure 6.35 produces 1 Hz square wave. Draw the signal shape at the output of op amp 1 and 2 provided the electrode connected to the input V_1 falls off.
9. Draw a circuit comprising three resistors and two DC voltage sources that is – examined from the output – equivalent to the circuits shown in Figure 6.31.
10. Compare the two definitions of P^+ (eq. 4.4 and eq. 4.5).
11. The selectivity of QRS detection is 97%. How many QRS complexes remain undetected in a 10-minute record if the heart rate is 60/min?
12. Solve Problem 11 if the heart rate is 90/min.
13. All parameters are the same as in Problem 11 but the record is 24-hour long (Holter monitoring). How many QRS complexes remain undetected?
14. The positive predictivity of QRS detection is 96%. How many segments will be in a 10-minute record falsely qualified as QRS if the heart rate is 60/min?
15. Solve Problem 14 if the heart rate is 90/min.
16. Solve Problem 14 for 24-hour Holter monitoring.
17. Select the 'depolarization' option in the 'Heart' menu of the ECGSIM program. Select a point on the ventricular wall and modify the parameters of its action potential in the 'TMP' window. Switch on the display of chest electrodes by selecting 'Heart' → 'show' → 'show electrodes'. Evaluate the changes in different leads caused by modifying the action potential parameters.
18. Prove that only two of the six frontal leads are independent provided Einthoven's hypotheses are valid.
19. We calculate the relation between frontal leads and find that $I + III = (1 + \alpha)II$. What can be the reason if $\alpha \neq 0$?
20. The low corner frequency of an ECG amplifier is 0.05 Hz (-3 dB). Calculate the resulting phase shift on 0.5 Hz.
21. Calculate the resulting phase shift of the amplifier in Problem 20 on 1 Hz.
22. The input symmetrical amplifier of an ECG equipment has a gain equal to 8. Following DC decoupling the gain of the main amplifier is 125. The decoupling circuit is a second order Butterworth high pass filter with corner frequency 0.05 Hz. Draw the wave shape on the output of the main amplifier when the input symmetrical signal is 1 Hz square wave with 1 mV amplitude and no common input voltage is present.
23. Draw the output voltage according to Problem 22 if the input symmetrical voltage is a 1 Hz triangle wave with 1 mV amplitude.
24. Draw the output voltage according to Problem 22 if the input symmetrical voltage is a 1 Hz sine wave with 1 mV amplitude.

25. The propagation of depolarization in the heart is slowest in the AV node. Why is it advantageous? How does it help the pumping function of the heart? How can we analyse the propagation speed of depolarization in the AV node?

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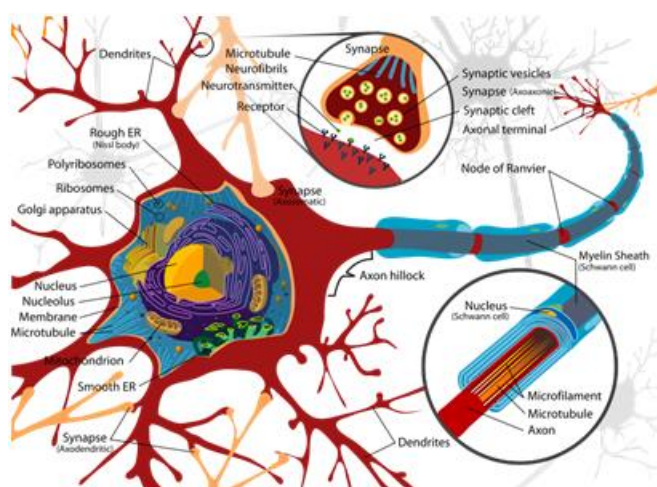
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Chapter 7. Electroencephalography

1. The structure to be analysed

Electroencephalography (EEG) analyses the electrical activity of the brain cells: about 10^{11} neurons and about 10^{12} glial cells [7.1]. It follows that only resultant activity of an area can be assessed by scalp electrodes. Figure 7.1 shows the basic structure of a nerve cell. The inputs are the dendrites. Signals arriving to the dendrites can cause the cell to ‘fire’: produce action potential on the axon which is the output of the cell. Once the change on the output has started it does not depend on the input signal any more. The shape of the output signal (action potential) is always the same independent of the input signal.

Figure 7.1. The basic structure of a nerve cell
http://hu.wikipedia.org/w/index.php?title=F%C3%A1jl:Complete_neuron_cell_diagram.svg&filetimestamp=20080501122856#file (author: Mariana Ruiz Villarreal)



Neurons have connections (synapses) with $10^3 - 10^4$ other neurons. The brain network is rather complex. The history of EEG analysis is described in [7.9].

2. Standardisation

Evaluation (also reproducibility and comparability) of EEG records is helped by defining the electrode positions on the scalp. In 1958 Jasper suggested defining the electrode positions percentually which can be applied to any size or form of the skull [7.2]. The placement of scalp electrodes is illustrated in Figure 7.2. The notifications are: Fp: frontopolar, F: frontal, C: central, P: parietal, O: occipital, T: temporal. C is only for identification, the other letters identify lobes. Two anatomical landmark points, nasion and inion, are used for positioning. Along the centre line between the nasion (right above the bridge of the nose) and the inion (the most prominent projection of the occipital bone at the lower rear part of the skull) there are three electrode positions with index z: Fz, Cz, Pz. 20% to the left from the centre line there are five electrode positions: Fp₁, F₃, C₃, P₃ and O₁. 20% to the right of the centre line there are also five electrode positions: Fp₂, F₄, C₄, P₄ and O₂. 40% to the left from the centre line there are three electrode positions: F₇, T₃ and T₅. 40% to the right of the centre position there are also three electrode positions: F₈, T₄ and T₆. Figure 7.3 shows the single plane projection of the head with the electrode positions. For research purposes laboratories use even more electrodes, e.g. also in the 5% positions [7.3].

Figure 7.2. The 10-20 electrode system suggested by Jasper (author: Jasper HH [7.2])

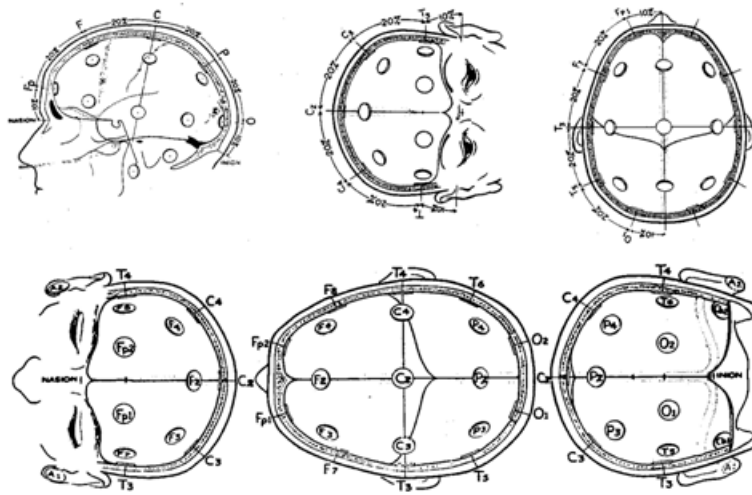
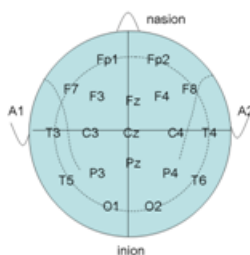


Table 7.1. Frequency ranges of EEG waves

Name of the wave	Frequency range of the wave, Hz
delta	0.5 - 4
theta	4 - 8
alpha	8 - 13
beta	13 - 30
gamma	30 - 80 (100)

Figure 7.3. The 10-20 electrode positions suggested by Jasper projected on a single plane
<http://de.wikipedia.org/w/index.php?title=Datei:10-20.PNG&filetimestamp=20070607121544> (author: Kok A)



The evaluation of the recorded signals starts with determining the dominant frequencies. It must be emphasised again that the electrical activity of an area is assessed by an electrode, if a dominant frequency exists it characterises the functioning of a great number of cells. Within that area the activity of a single cell can be quite different from the resultant one. The usual frequency ranges are given in Table 7.1. There are other frequency ranges for classification of EEG waves: e.g. the delta range includes also the theta range, or the alpha, beta and gamma range can be split in two subranges (e.g. alpha1 8 – 10 Hz and alpha2 10 – 13 Hz, beta1 13 – 20 Hz, beta2 20 – 30 Hz, gamma1 30 – 40 Hz, gamma2 >40 Hz). Delta wave is typical during deep sleep, theta waves occur during the REM (rapid eye movement) phase of sleep. Alpha waves characterise the relaxed state: the person is awake, at rest, eyes closed, slow mental activity. Beta waves characterise a person with a concentrated mental activity (e.g. problem solving), strong environmental stimuli. Beta waves are also present in the REM phase of sleep. Gamma waves are related to cognitive functions. During the meditation of experienced persons

(Tibetan Buddhist monks) correlation were found between transcendental mental states and gamma waves [7.4]. Further details can be found on EEG signals in [7.10]. EEG records can be freely downloaded [7.11]. The [7.12] database contains normal and pathological EEG signals. Noises and disturbances during the records (eye movement, blinking, chewing, bad electrode contact, and power line noise) are described and their effect is illustrated.

3. Evaluation of EEG records

The first EEG record was taken by Hans Berger in 1924. He described the delta, theta, alpha and beta waves first. Gamma waves were identified later. Evaluation depends on the purpose of the record taken. At present experts agree that EEG reflects the electrical activity of cell groups but no thoughts can be decoded. The purpose of EEG taking EEGs can be

- to determine the level of alertness and the sleep phases,
- diagnosing epilepsy, separating epileptic seizures from other neurological disorders (e.g. migraine),
- location of electrically inactive areas: necrosis, coma,
- affirmation of brain death (electrocerebral silence).

In the process of diagnosing (locating) tumour or stroke MRI and CT offers better spatial resolution than EEG. On the other hand, EEG is much better in the time domain. Its resolution easily reaches 1 ms which is possible neither for MRI nor for CT. Figure 7.4 shows the phases of sleep of a young healthy person.

Figure 7.4. Phases of sleep http://en.wikipedia.org/wiki/File:Sleep_Hypnogram.svg (author: Razer M)

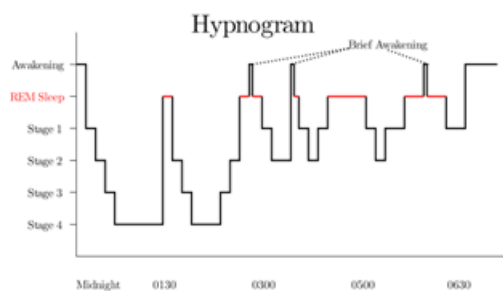
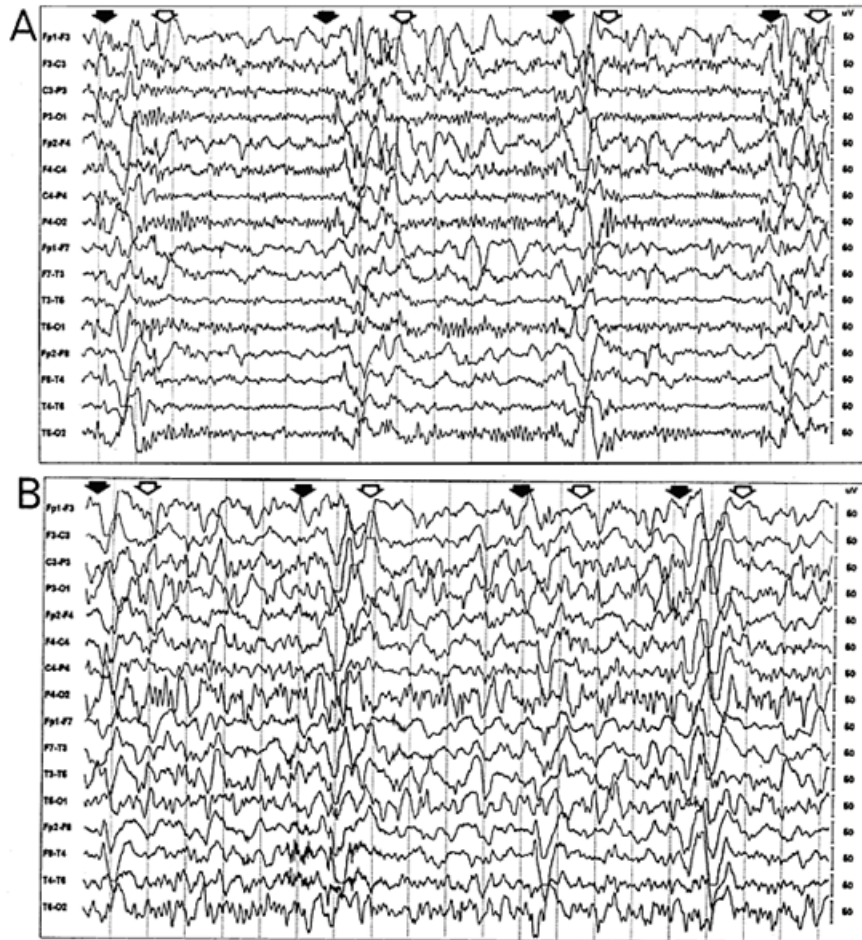


Figure 7.5 shows records taken from a patient with Dawson encephalitis (subacute sclerosing panencephalitis). Three months have passed between records A and B. Arrows point to the onset (dark arrows) and offset (open arrows) of low frequency high amplitude complexes [7.5]. Slowing down of background activity is present only in the frontal leads of record A. In three months the patient's state worsened. The background rhythm diffusely slowed down, low frequency activity hardly arises from it.

Figure 7.6 shows the effect of eye opening on the EEG.

Figure 7.5. EEG record from a patient with Dawson encephalitis. The interval between adjacent vertical lines is 1 s. <http://commons.wikimedia.org/wiki/File:Bonthius2b.gif> (authors: Bonthius D, Stanek N, Grose C [7.5])



Early EEG records were plotted or printed on numbered sheets of continuous paper. Visual evaluation was common practice. The medical doctor performed ‘signal processing’ an engineer would call determining dominant frequency, pattern matching and symmetry search.

For computer aided EEG evaluation the Fourier analysis is not optimal. The reason is that the Fourier transformation determines the frequency components over the whole record; it is unable to locate patterns with given frequency range within a time window. Figure 7.7 shows an example. In this figure there is a short, 1-s 9 Hz spindle. The other part of the record the signal amplitude is negligible compared to the amplitude of the spindle. Such spindles are frequently present in the EEG signal. Fourier analysis is done with 8-s time window the time step is 1 s. This means a 7/8 overlap between adjacent windows. While the 1 s spindle is within the 8-s window the frequency spectrum remains the same (Figure 7.7 upper subfigure).

Figure 7.6. The effect of eye opening on the EEG signal
http://commons.wikimedia.org/wiki/File:EEG_Opening_eyes.png (author: Otoomuch)
http://www2.massgeneral.org/childhoodepilepsy/medical/diagnosis-popup_general.htm



Berg transform [7.6] uses different window lengths to identify the different frequency components. The formulas used for the transform:

$$A_n = \frac{k_1}{T_m} \int_0^{T_m} f(t) \cos(2\pi f_n t) dt \quad (7.1)$$

$$B_n = \frac{k_1}{T_m} \int_0^{T_m} f(t) \sin(2\pi f_n t) dt \quad (7.2)$$

$$T_m = \frac{k_2}{f_n} = k_2 T_n \quad (7.3)$$

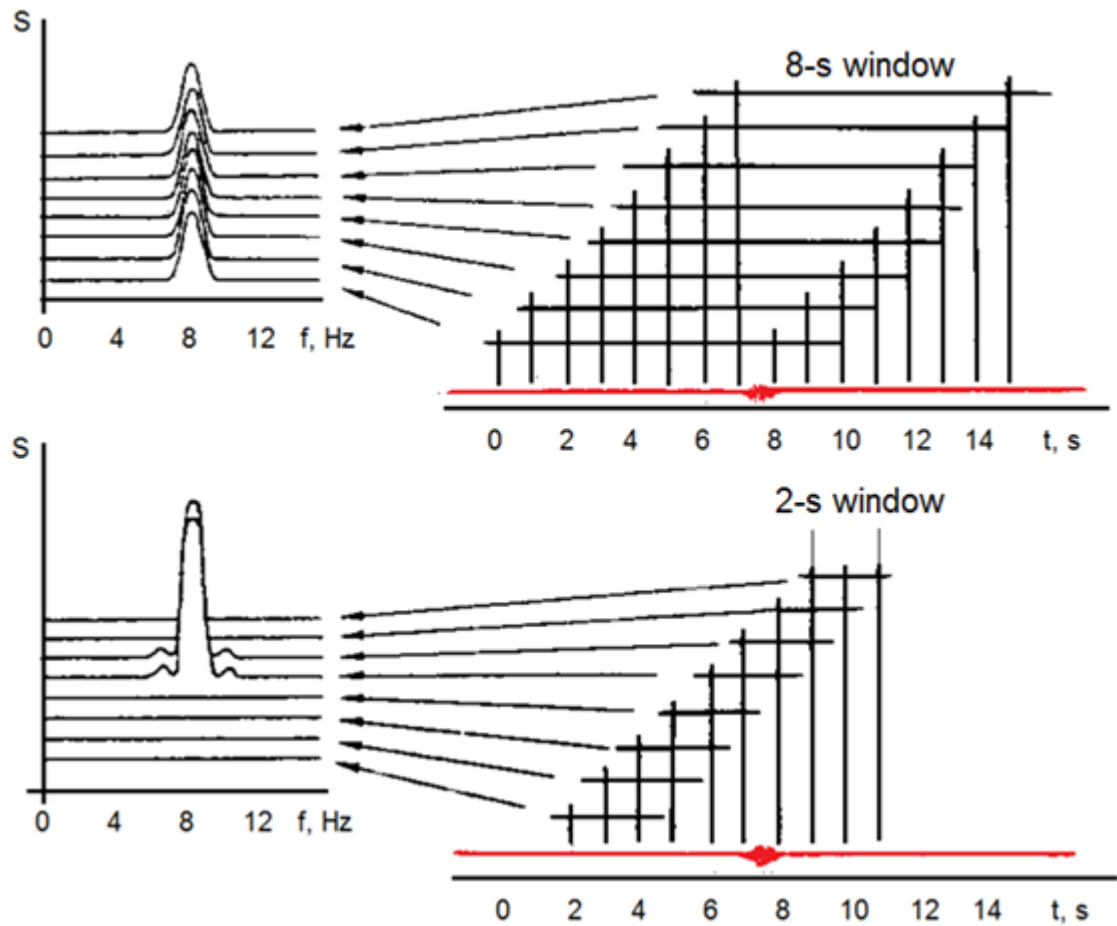
$$C_n = \sqrt{A_n^2 + B_n^2} \quad (7.4)$$

The length of the time window (T_m) compared to the time period (T_n) of the frequency component to be analysed is set by constant k_2 . Consequently, the relative frequency resolution is given by eq. 7.5.

$$\frac{f_n}{\frac{1}{T_m}} = k_2 \quad (7.5)$$

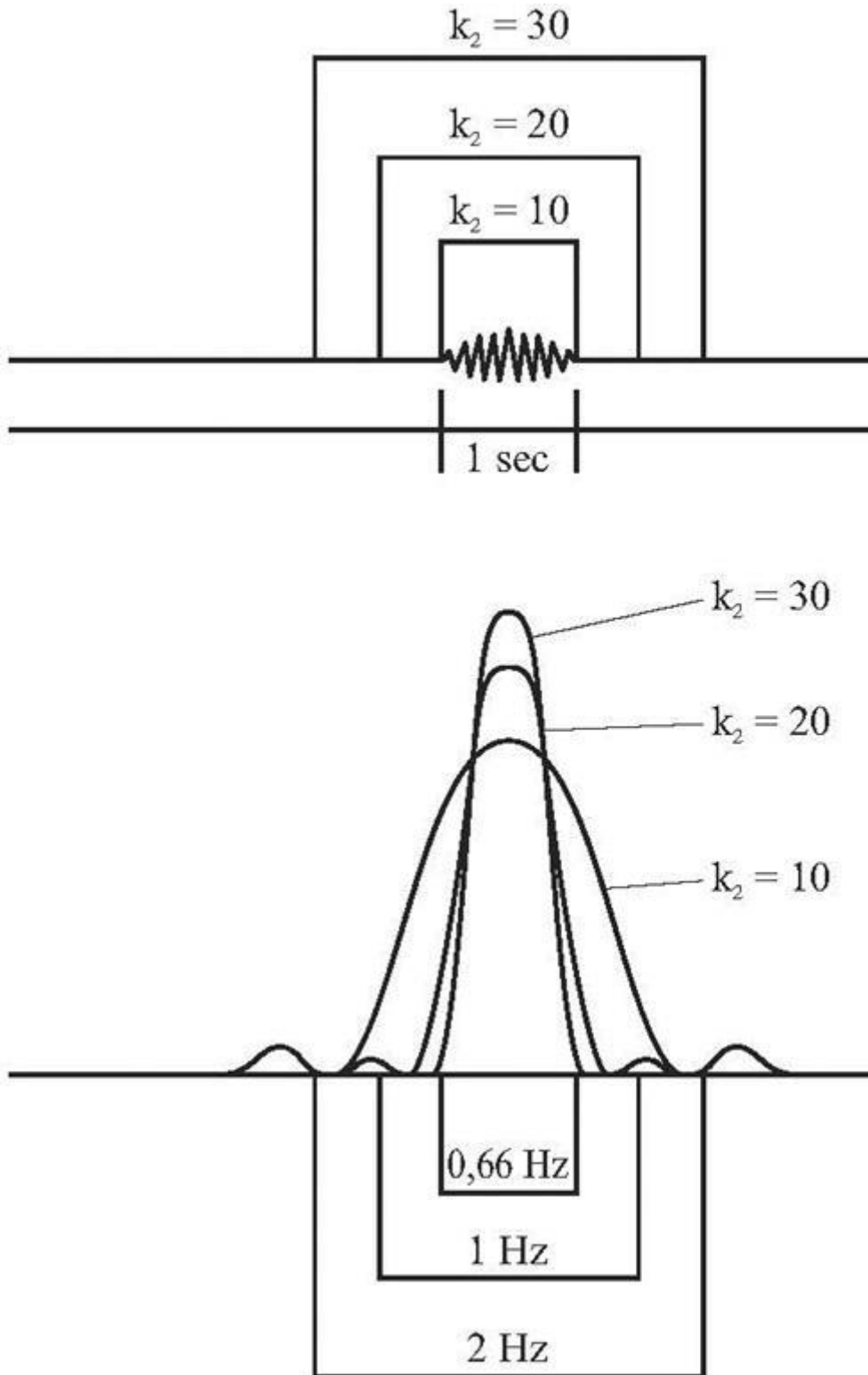
Short time window assures high resolution in time, but in this case the frequency resolution is coarse.

Figure 7.7. Evaluation of the EEG record using Fourier (top) and Berg (bottom) transform. The signal to be analysed is in red.



The bottom subfigure in Figure 7.7 shows how the 10 Hz component is located with the Berg transform. $k_1 = 1$ and $k_2 = 20$, so the time window is $T_m = 2$ s. Figure 7.8 shows how a 1 s long 10 Hz signal appears in the spectrum according to different k_2 values. A single spectrum line (in this example at 10 Hz) would need an infinite long record. When $k_2 = 10$ then $T_m = 1$ s and the frequency resolution is 1 Hz. When $k_2 = 20$ (30) then $T_m = 2$ (3) s and the frequency resolution is 0.5 (0.33) Hz.

Figure 7.8. Increasing the resolution in time widens the line in the frequency spectrum



Wavelet analysis fits well to analyse evoked potentials [7.7] and to identify spikes during epileptic seizures [7.8]. Evoked potential of the brain has much smaller (typically by an order of magnitude) amplitude than normal EEG. The stimulus is repeated several times and the recorded signal is averaged synchronised to the stimulus. This enhances the evoked potential if other brain activities are not correlated with the stimulus. Synchronisation to stimulus makes the application of wavelet analysis more effective.

Autocorrelation and cross correlation are frequently used for the evaluation of EEG signals. The former can reveal regularity in a signal the latter finds relation between two signals. Autoregressive modelling of EEG assumes the signal as the sum of a stationary background process and several transient processes.

The square of the EEG signal is related to activity, the first derivative to mobility and the second derivative to complexity.

4. Devices

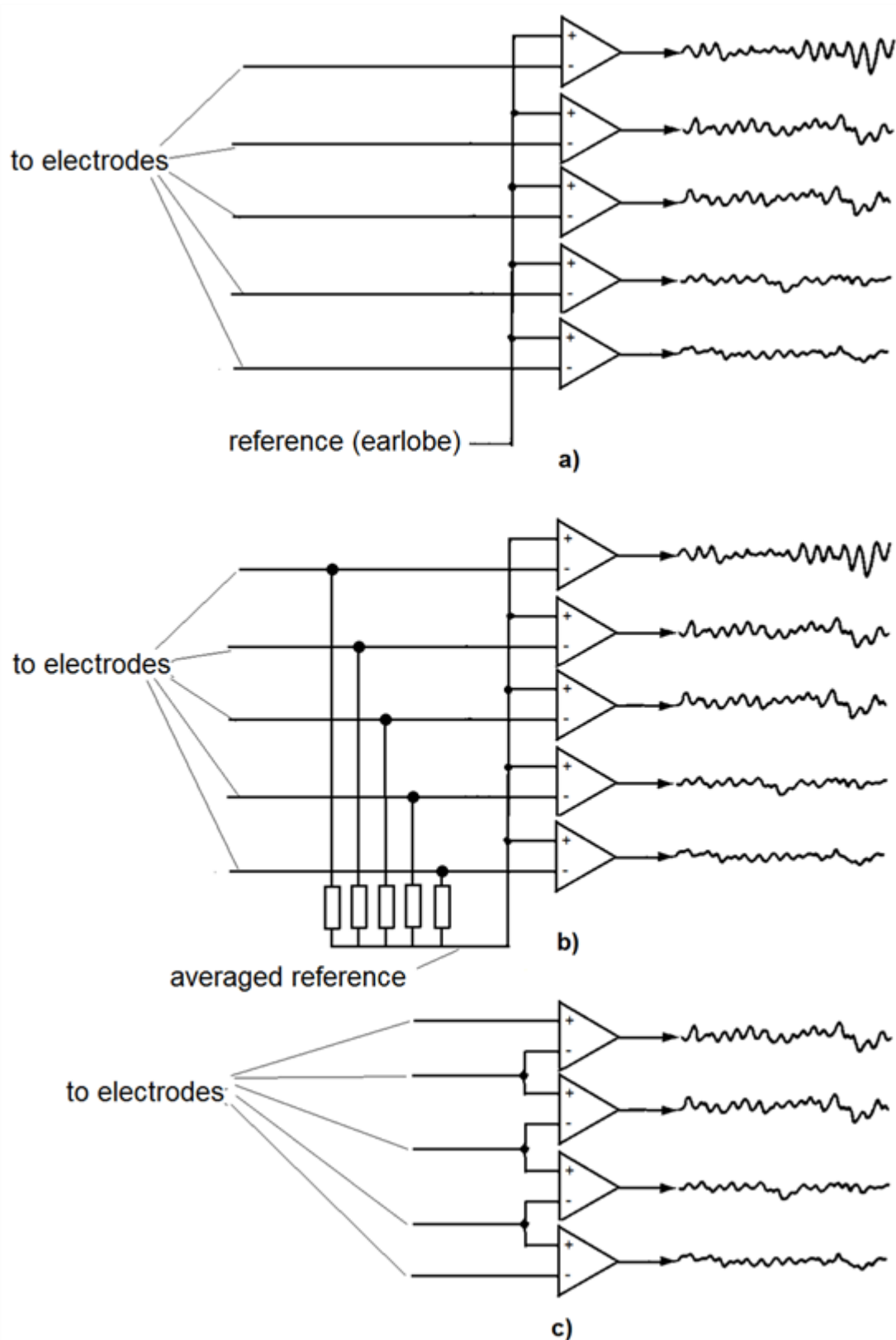
Figure 7.9 shows the three possible lead types that can be configured using scalp electrodes. Unipolar lead (Figure 7.9.a) requires a reference point. Most often this is the earlobe because the electrical activity of brain cells influences its potential only negligibly. The electrical activity can be located easily if its amplitude is big and its source is not too close to the reference point. Activity close to the reference point is present in all channels thus locating it is difficult. It is important to note that the reference is not a guard!

The averaged unipolar lead (Figure 7.9.b) generates the reference potential from the signals of all electrodes by using identical resistors (of high value). In each channel the potential difference between the related electrode and the reference can be measured. Electrical activity limited to a small area will be present in a few channels.

The bipolar lead (Figure 7.9.c) is the potential difference of two electrodes. These leads help locate the electrical activity of a small area. Activity close to an electrode will produce positive pulse in one lead and negative in another.

The insulation of the skull attenuates electrical potential of brain cells. Thus the EEG signal amplitude is low; the typical input range is $1 - 100 \mu\text{V}$. Power line noise is present on the scalp as well with amplitude of a few volts. The EEG device must have a very high CMRR; 140 dB is typical. The maximum gain is 10^6 (120 dB). The gain can be adjusted jointly for all channels and selectively for each channel. Per channel gain can usually be set in fix steps, the ratio of maximum/minimum gain is around 500. The bandwidth of a channel can be set according to the actually measured signal. The bandwidth should be limited to the necessary value to increase signal/noise ratio. Low corner frequency can usually be set per channel in the range $0.1 - 5 \text{ Hz}$. The high corner frequency range is typically $15 - 100 \text{ Hz}$. The input resistance must be high ($R_{\text{in}} = 1 - 10 \text{ M}\Omega$) and the input capacitance must be small ($C_{\text{in}} = 2 - 10 \text{ pF}$) to assure high input impedance not to attenuate the input signal.

Figure 7.9. Unipolar (a, b) and bipolar EEG leads



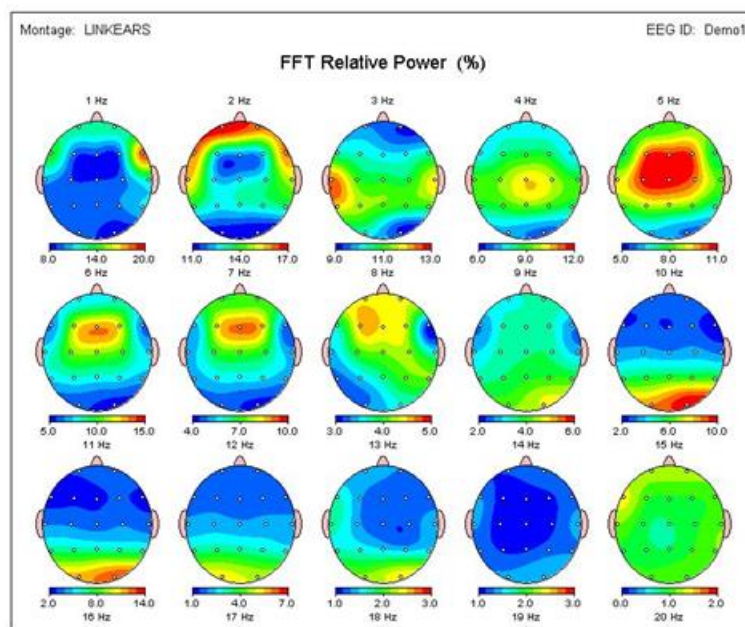
Checking the skin-electrode contact is necessary in diagnostic EEG equipment. Continuous monitoring (like in an ECG) is not possible because of the necessary high CMRR. Electrode contact measurement is usually a selectable operating mode different from measuring mode.

Head box helps connecting the EEG cables. Located close to the scalp short electrode cables can be plugged into it. Short cables have low capacitances and form small area thus the picked-up noise is low. The head box shows the top-view of the scalp; its connectors are labelled as the electrode positions.

Recorded data can be displayed both in time and in frequency domain. Time functions of the channels are displayed one below the other. The frequency spectra of channels (calculated for disjunctive or overlapping time windows) are usually drawn one behind the other so changes can easily be seen. EEG map means an artificially coloured map based on the activity. Mapping helps locate inactive areas. Figure 7.10 shows activity distribution calculated for different frequencies (1 – 15 Hz).

EEG devices are often used together with light or sound stimulators. They provide trigger (synchronisation) signal to help averaging of evoked potentials. Nevertheless, it must be noted that neither assumptions are completely true needed for effective improvement of signal-to-noise ratio by averaging. The two assumptions are the following: (a) the time delay between stimulation and the appearance of evoked potential is constant, (b) background activity and activity resulting from stimulation are completely uncorrelated even after a number of stimulations.

Figure 7.10. EEG mapping of recorded data
<http://www.appliedneuroscience.com/index.html> (author: Applied Neuroscience Inc.)



Light stimulators are able to provide two flashes with a delay time less than 1 ms. Possible operating modes:

- 100 Hz frequency free running (astable),
- variably frequency (1 – 50 Hz) free running (astable),
- single pulse mode,
- double pulse mode,
- pulse burst,
- single (manual) pulse,
- synchronisation to external signal.

Sound stimulators have volume control. Possible operating modes:

- fix frequency sound, usually 250, 500, 1 k, 2 k and 5 kHz,

- modulation with 2 – 20 Hz,
- random pulses (with given statistical parameters),
- synchronisation to external signal.

Using stimulators and evaluating the EEG makes possible diagnosing the patient's sense organs, nerve tracts and brain areas without cooperation.

5. Problems

1. 8 – 13 Hz spindles are searched for in a 20-minute record. What is the minimum length of the applied time window if the required frequency resolution is 0.2 Hz?
2. The amplitude of the EEG signal to be measured is 10 μV ; the amplitude of the signal deriving from the power line on the patient's body surface is 1 V. Calculate the signal-to-noise ratio on body surface in dB.
3. The signal on the body surface described in Problem 2 is led to an amplifier with 140 dB CMRR. Calculate the noise amplitude/signal amplitude in percentage in the output signal. (The noise of the amplifier can be neglected, no filtering is applied, and the amplifier is not saturated.)
4. What is the disadvantage of applying Fourier transform to evaluate EEG signals in the frequency domain?
5. What changes will be caused by a bad skin-electrode contact in the three different EEG leads (see Figure 7.9)? What will be the result if the bad contact is at the reference electrode (Figure 7.9.a)?

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Chapter 8. Measuring blood pressure and blood flow

Blood pressure is one of the most important physiological parameters. Seemingly it is easy to measure – in fact it is not. Blood pressure is the pressure exerted by blood to the walls of vessels. It has three components: static, hydrostatic and kinetic. Medical doctors are interested in the static (hemodynamic) pressure. This is determined by the heart (the stroke volume pumped from the left ventricle), the stiffness of arteries and the peripheral resistance. Without special notice the blood pressure characteristic for a person is defined at the level of the heart (left ventricle). Hydrostatic pressure arises if the measurement is done at a different height. When the upper arm is held horizontally (in line with the shoulder, sitting person) then the measured blood pressure is about 15 mmHg less than the actual one. Blood pressure difference caused by blood flow is usually negligible.

In 1837 Stephen Hales in his essay *Haemestatics* published his experiments demonstrating the pulsation of blood pressure (see Figure 8.1).

Figure 8.1. Stephen Hales demonstrates pulsation of blood pressure in the jugular artery <http://www.mcgill.ca/files/library/OLN114.pdf> (author: Macklem PT [8.1], the original figure is from *Medical Times* 72 (1944) 11.)



In the nineteenth century constructed the sphygmograph (today such equipment is called tonometer) which was able to record the blood pressure – time function of the radial artery [8.2]. In 1896 Scipione Riva-Rocci published the basics of the cuff-based mercury sphygmomanometer. The non-invasive blood pressure measurement is based on the published measurement principle to this day. Invasive blood pressure measurement requires surgical intervention. Further details about the history of blood pressure measurement can be found in [8.3], [8.4], [8.5], [8.6], [8.7] and [8.8]. The reliability and accuracy of cuff less non-invasive blood pressure measurement [8.9], [8.10], [8.11], [8.12] falls short to the level needed to widespread application.

Different invasive and non-invasive measurement methods of flow and volume of blood are known. The accuracy of non-invasive methods is enough for qualitative assessment which is adequate for present-day diagnostic and therapeutic procedures.

1. Factors influencing blood pressure

Blood flow is sustained by the heart. In the atria and ventricles of healthy adults the typical blood pressure values are in the ranges given in Table 8.1.

Table 8.1. Typical pressure values in the atria, ventricles an aorta of healthy adults [8.22]

right atrium	1 – 6, average 4 mmHg
left atrium	2 – 12, average 8 mmHg
right ventricle	end diastole: 4 mmHg, maximum during systole: 24 mmHg
left ventricle	end diastole: 8 mmHg, maximum during systole: 120 mmHg
aorta	80 – 120 mmHg
aorta pulmonalis	9 – 24 mmHg

Along the blood vessels blood pressure is different. At a given point it changes in time. Usually the blood pressure of a person is characterised by two pressure values (e.g. 120/80 mmHg). This implies that the measurement was taken on the upper arm at the level of the left ventricle and at that level the blood pressure changes between constant minimum and maximum values. The first numerical value is the systolic pressure, the maximum blood pressure at the level of measurement. The second numerical value is the diastolic value, the minimum blood pressure at the level of measurement. Usually at a given point of the artery the maximum and minimum values are not constant. Figure 8.2 shows the blood pressure-time function recorded with a tonometer at the radial artery of a young healthy male. The systolic and diastolic values (maximum and minimum values in a heart cycle) can be markedly different even in two adjacent heart cycles. The blood pressure of a person in general cannot be characterised by two numerical values only. The movie http://project.mit.bme.hu/kobak2012/Invasive_bloodpressure_monitoring.wmv shows the blood pressure of a patient in an intensive care unit. The invasive sensor was introduced into the femoral artery. Within a minute the systolic pressure fluctuates between 137 and 152 mmHg, the diastolic between 75 and 84 mmHg. Table 8.2 lists activities that can influence blood pressure substantially [8.13]. During blood pressure measurement the tested persons should be at rest; their stress level should be low. The results can be compared when they are taken at the same phase of daily activity. At home blood pressure should be taken in the morning, right after waking up.

Figure 8.2. Blood pressure – time function taken by a tonometer on the radial artery of a young healthy male

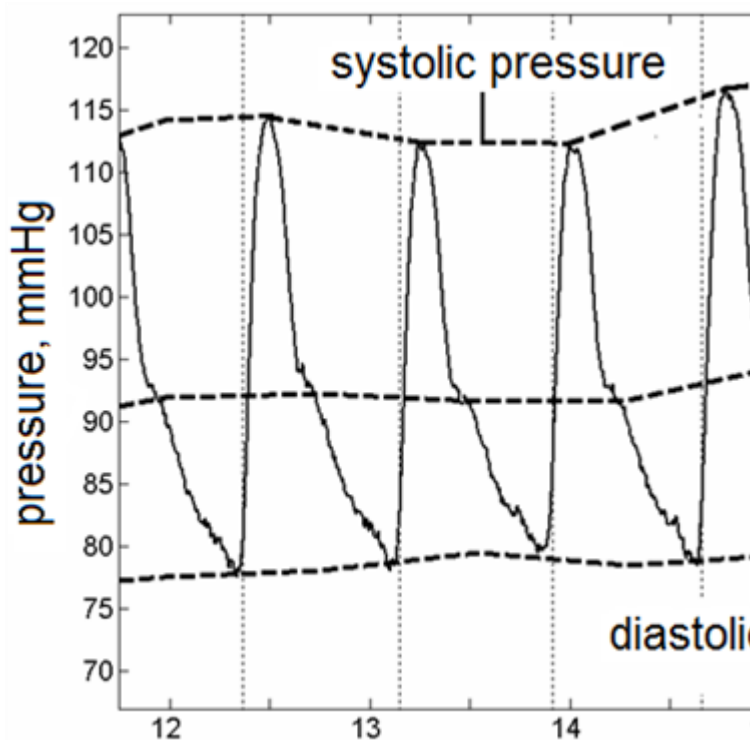


Table 8.2. Activities that can influence blood pressure substantially

activity	change (systolic/diastolic), mmHg
meeting	+20/15
rendezvous	+20/15
physical activity	+16/13
walking	+12/6
meals	+9/10
sleep	-10/8

Body weight substantially influences blood pressure [8.14].

Factors influencing blood pressure in arteries:

- stroke volume (the volume of blood pumped from the left ventricle in one heart cycle),
- elasticity of arterial wall,
- geometry of artery.

Blood pressure at a given point (eq. 8.1):

$$p_t = p_s + \frac{1}{2}\rho v^2 + \rho gh \quad (8.1)$$

where p_s is the static pressure, $\rho v^2/2$ is the pressure caused by blood flow and ρgh is the hydrostatic pressure. The aim of blood pressure measurement is to determine p_s . The effect of hydrostatic pressure is eliminated if the pressure sensor (cuff) is at the level of the left ventricle. If the sensor is higher than the heart then the pressure measured is 1 mmHg lower by each 1.3 cm. If the sensor is lower than the heart then the measurement results in higher values than the actual. The pressure resulting from blood flow is less than 1 mmHg thus it can be neglected. (Supposing the density of blood is 1 kg/dm³, the rate of flow in the brachial artery is 0,5 m/s then the pressure resulting from flow is 0,94 mmHg.) The pressure sensors for invasive measurement are side mounted at the tip of the catheter. Figure 8.3 shows a catheter for mice. Its diameter is 0.36 mm (1.1F), at the tip it is 0.46 mm (1.4F). The pressure sensor is 2 mm from the tip perpendicular to the centre line of the catheter.

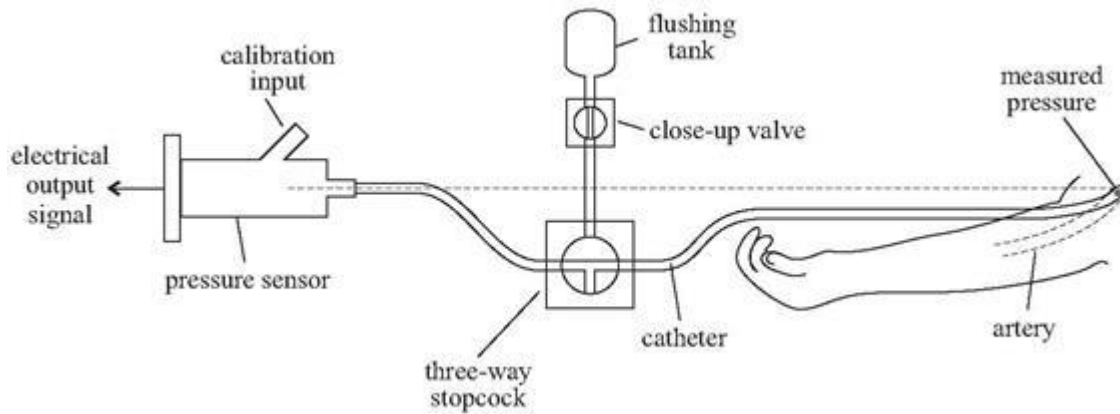
Figure 8.3. Intraarterial pressure sensor for mice (ADInstruments, SPR-671 Millar Mikro-Tip) (top), the sensor window enlarged (bottom)



2. Direct (invasive) blood pressure measurement methods

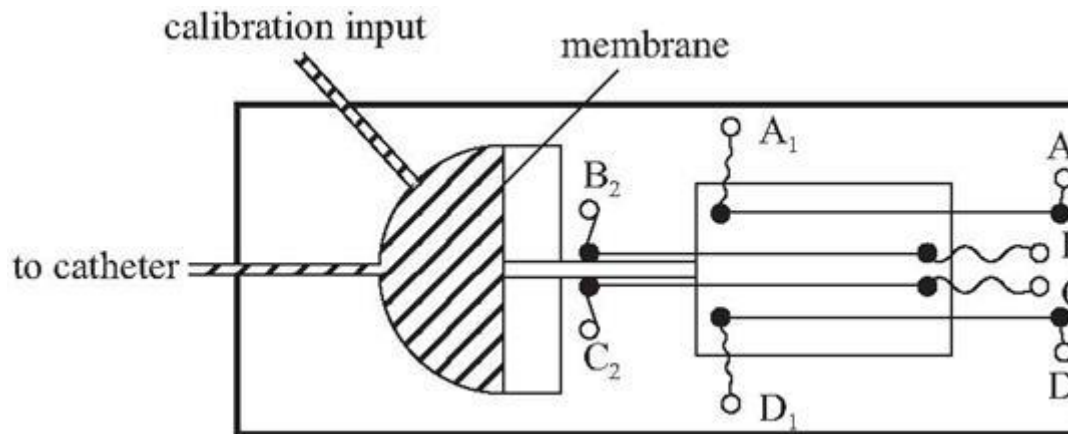
During direct (invasive) blood pressure measurement the sensor can be inside (see Figure 8.3) or outside the artery. In the latter case a fluid-filled catheter connects the inner point to the sensor. The usual set-up is given in Figure 8.4. Figure 8.5 gives a possible scheme of the pressure sensor. Both the sensing point (one end of the catheter) and the pressure sensor must be at heart level (see dashed line) to eliminate the hydrostatic component. The three-way stopcock connects the pressure sensor either to the catheter introduced into the artery or to the flushing tank. In this latter position bubbles can be removed and the sensor can be calibrated. Connecting the flushing tank to the catheter to the artery coagulation can be prevented.

Figure 8.4. Invasive blood pressure measurement set-up with external pressure sensor



In the sensor shown in Figure 8.5 pressure increase shifts the membrane to the right. This decreases the resistance of the A (between A_1 and A_2) and D (between D_1 and D_2) wires while increases the resistance of the B (between B_1 and B_2) and C (between C_1 and C_2) wires. The resistances of the wires (strain gauges) can be measured using the circuit shown in section 2.1.3.

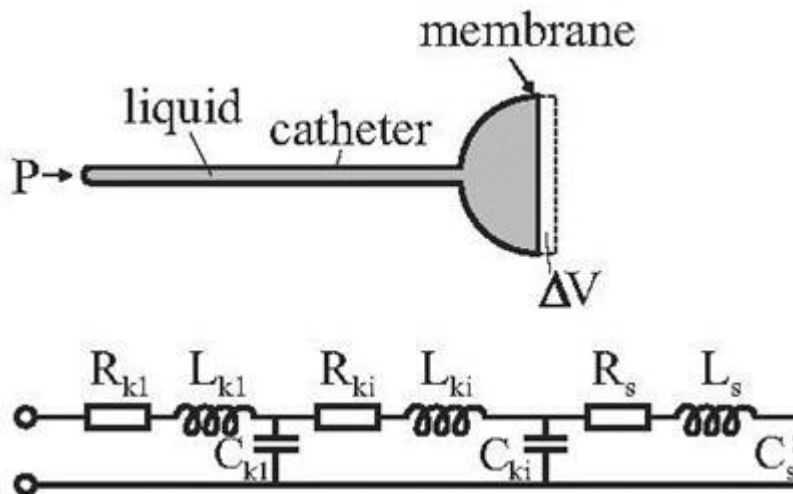
Figure 8.5. A possible construction of a pressure sensor with four strain gauges



The electrical model of invasive blood pressure measurement using a catheter is shown in Figure 8.6. The i^{th} segment of the catheter has resistance R_{ki} , inductance L_{ki} , and compliance C_{ki} . The sensor is modelled by R_s , L_s and C_s . The compliance of the membrane is C_m . The transfer function from the tip of the catheter within the artery to the pressure sensor is low pass type. The resistances model the friction of molecules during flow; the inductances model the mass of blood in the compartments and capacitors model the elasticity of vessel walls [8.25]. It is important that bubbles get neither into the catheter nor into the arteries. A bubble in the circulation is a life threatening situation. Bubbles in the catheter forms a low-pass filter and thus distorts the measurement result. A catheter free of bubbles has a transfer function with high corner frequency about 10 – 20 Hz. When bubbles get into the catheter the high corner frequency drops by an order of magnitude [8.2].

Analysis of blood pressure – time functions revealed that the 6th – 10th harmonic is needed to keep the wave shape. This requires at least 15 – 20 Hz high corner frequency for the catheter, too.

Figure 8.6. Electrical model of invasive blood pressure measurement using catheter



When the sensor is within the artery there is no need for hydraulic connection through a catheter. High frequency components of the signal can be recorded. Different pressure sensor types can be fabricated in a miniature size allowing insertion into the vessels. A possible structure is shown in Figure 8.3.

Reusable blood pressure transducers use external sensors. Disposable transducers minimise the risk of interpersonal infection. These are usually cheap, semiconductor-based transducers.

For patients with cardiovascular diseases of high risk (e.g. high blood pressure and cardiac decompensation) the long-term (even for weeks) invasive blood pressure monitoring may be required. A reasonable solution can be using implantable sensor with wireless communication [8.15]. In animal studies sensors with cuffs circling the artery are used in an effective way. The cuff does not occlude the vessels completely. The artery must have at least 1 mm diameter. Using flat sensor attached to the vessel wall the blood pressure can be monitored down to 0.2 mm diameter [8.16].

3. Indirect blood pressure measurement methods

The majority of indirect blood pressure measurement methods are cuff based. The classic indirect method requires the occlusion of the artery – most often on the upper arm – by an external cuff. The pressure of the cuff is continuously changed and monitored. When the cuff pressure is higher than the systolic pressure then the artery is completely occluded (during the whole heart cycle), blood flow is stopped. When the cuff pressure is lower than the diastolic pressure then artery is open, blood flows during the whole heart cycle. When the cuff pressure is between the diastolic and systolic pressure then in each heart cycle the artery opens for a while and then it is occluded for the rest of the cycle. There are different methods to identify when cuff pressure is equal to diastolic or systolic pressure. Detecting that cuff pressure is equal to systolic pressure the latter can be determined by measuring the former. The same is true for the diastolic pressure. This process was first published in 1896 by Scipione Riva-Rocci.

The cuff is inflated and deflated according to different programs. Too fast deflation of the cuff results in methodological error. This means that in one heart cycle the cuff pressure is higher than systolic pressure while in the next heart cycle it is lower. In case of too fast deflation the difference in cuff pressure is too high at two adjacent systolic pressures. Also, if the deflation is too fast then cuff pressure can only be compared to a single systolic pressure which may vary, see Figure 8.2. When the cuff is deflated too slowly then the tested persons would feel uncomfortable. This might elevate their systolic pressure. (The parameter to be measured changes as a result of the measurement!) The compromise is usually 3 mmHg/s deflation speed.

Observing the pulse wave

The pulse wave can be detected distal to the cuff until the artery is completely occluded. Pulsation of the artery can be determined by observing the blood flow (see section 4.2.2) or the movement of the arterial wall (e.g. with an ultrasound sensor, see Figure 8.7). The pulse wave can be detected also by palpation. Observation of the pulse wave helps determine the systolic pressure. When the cuff is deflated below the diastolic pressure there is no change in the pulse wave.

Observing the opening and closing of the blood vessel

The opening and closing of the vessel under the cuff can be detected (see Figure 8.7). The method is sensitive to the placement of the sensor. The ultrasound transmitter and receiver must be placed so that it can perceive both the opening and closing of the artery. This cannot be guaranteed with the same cuff and sensor for patients with different upper arm diameter. As a result, this method is not widely used.

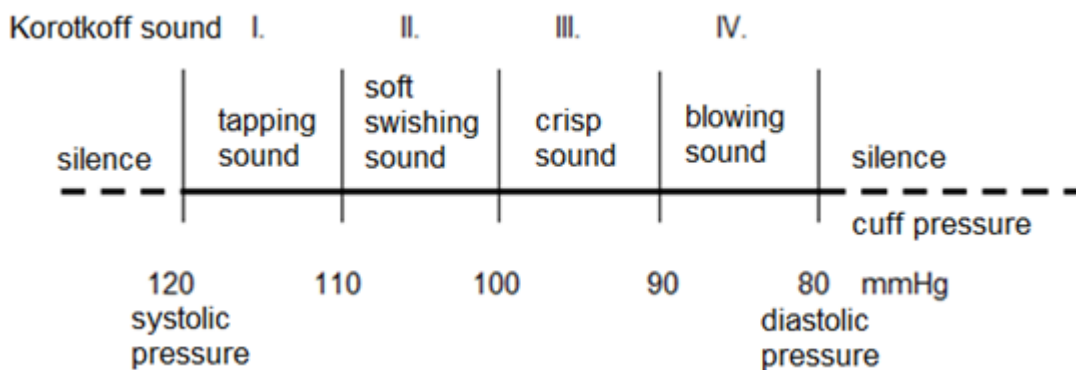
Figure 8.7. Ultrasound transmitter and receiver placed under the cuff to detect closing and opening of the artery



Observing the Korotkoff sounds

In 1905 Nikolai Sergeyevich Korotkoff published the characteristics of the sounds that can be heard by listening to the artery just below the cuff with a stethoscope while cuff pressure is slowly released from the systolic to the diastolic pressure of the person. When cuff pressure falls just below the systolic pressure the sudden distension of the artery and the resulting turbulent flow produce the first Korotkoff sound. As the pressure in the cuff drops further the artery is open for a longer time in a heart cycle producing different sounds (see Figure 8.8). The frequency ranges of the Korotkoff sounds are between 100 – 500 Hz. Application of a band pass filter helps identify the sounds.

Figure 8.8. The five types of Korotkoff sounds as a function of cuff pressure provided the blood pressure is 120/80 mmHg

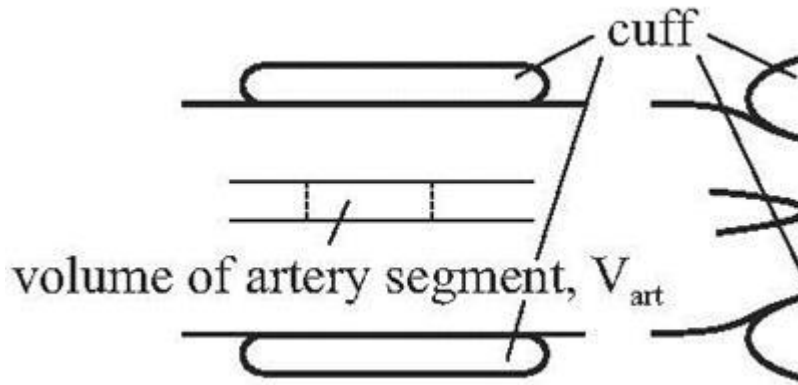


When the cuff around the brachial artery is inflated to a pressure above the patient's systolic blood pressure then no sounds can be heard in the stethoscope placed over the brachial artery just below the cuff. During deflation of the cuff the sounds appear while cuff pressure is between the patient's systolic and diastolic pressure. Figure 8.8 shows the sound types: silence – tapping – soft swishing – crisp – blowing – silence. The intensity increases during cuff deflation until the maximum during crisping and then it decreases. The method underestimates the systolic, and overestimates the diastolic pressure [8.17]. The main sources of error are: external noise and displacement of the microphone.

The oscillometric method

The pulse wave in the brachial artery causes oscillations in the cuff pressure (see Figure 8.15). These oscillations can be detected even when the cuff pressure is above the systolic or under the diastolic pressure. The equivalence of cuff pressure to systolic, diastolic and mean blood pressure is determined by measuring the oscillometric amplitudes. Semiautomatic and automatic blood pressure meters almost exclusively apply the oscillometric method because no extra sensor is needed; only the cuff pressure has to be monitored. Figure 8.10 shows the arterial volume (V_{arts} Figure 8.9) circled by the cuff as a function of the transmural pressure $P_{\text{trm}} = P_{\text{artery}} - P_{\text{cuff}}$.

Figure 8.9. Arterial volume circled by the cuff



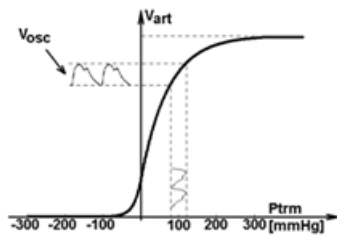
The vessel volume – transmural pressure curve is steepest when the cuff pressure equals to arterial mean pressure, p_m , (see Figure 8.11). Arterial mean pressure is defined in eq. 8.2.

$$p_m = \frac{1}{T} \int_0^T p(t) dt \quad (8.2)$$

where T is the length of one heart cycle. In case of typical blood pressure vs. time wave shape, the arterial mean pressure is twice as far from the systolic as from the diastolic pressure, see eq. 8.3.

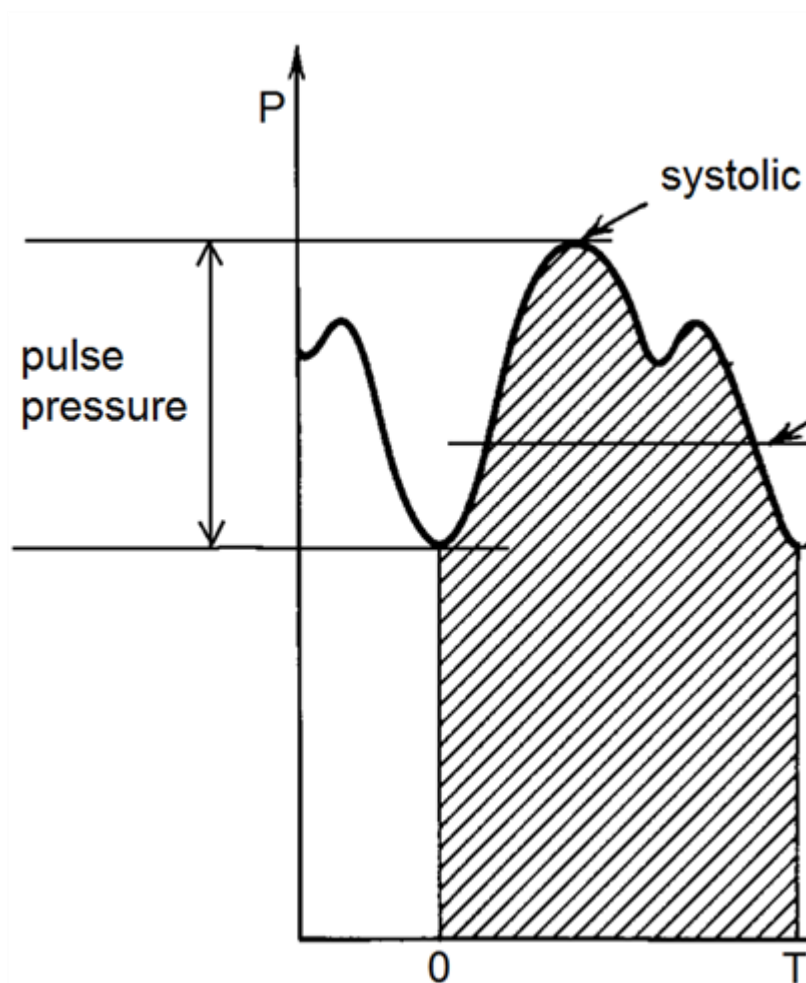
$$p_m \approx p_{dia} + \frac{1}{3}(p_{dia} + p_{sys}) \quad (8.3)$$

Figure 8.10. Arterial volume under the cuff (V_{art}) as a function of transmural pressure (P_{trm})



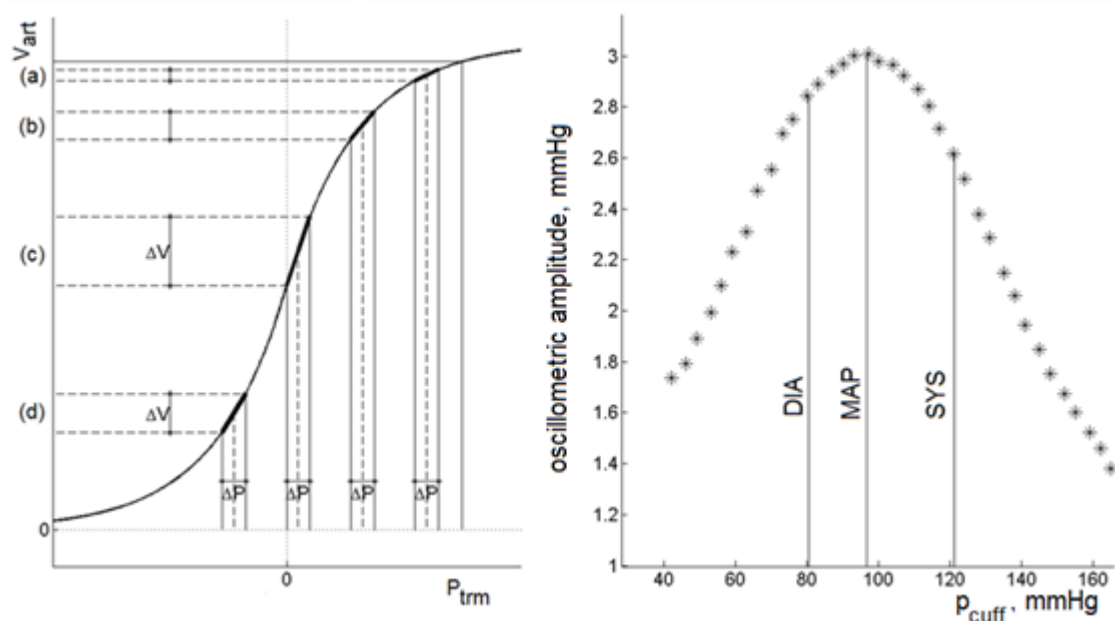
When the cuff is completely deflated then transmural pressure equals to blood pressure. The arterial volume under the cuff only slightly changes when blood pressure fluctuates between systolic and diastolic pressure (Figure 8.12, left subfigure, marked by 'a'). Increasing cuff pressure the same pulse pressure (pressure change from diastolic to systolic) results in bigger change in arterial volume under the cuff (Figure 8.12, left subfigure, marked by 'b'). The maximum change in V_{art} belongs to cuff pressure equal to arterial mean pressure (Figure 8.12, left subfigure, marked by 'c'). Further increasing the cuff pressure change in V_{art} decreases (Figure 8.12, left subfigure, marked by 'd'). The cross section of the artery changes as the cuff pressure changes (see Figure 8.13).

Figure 8.11. Blood pressure vs. time in the artery



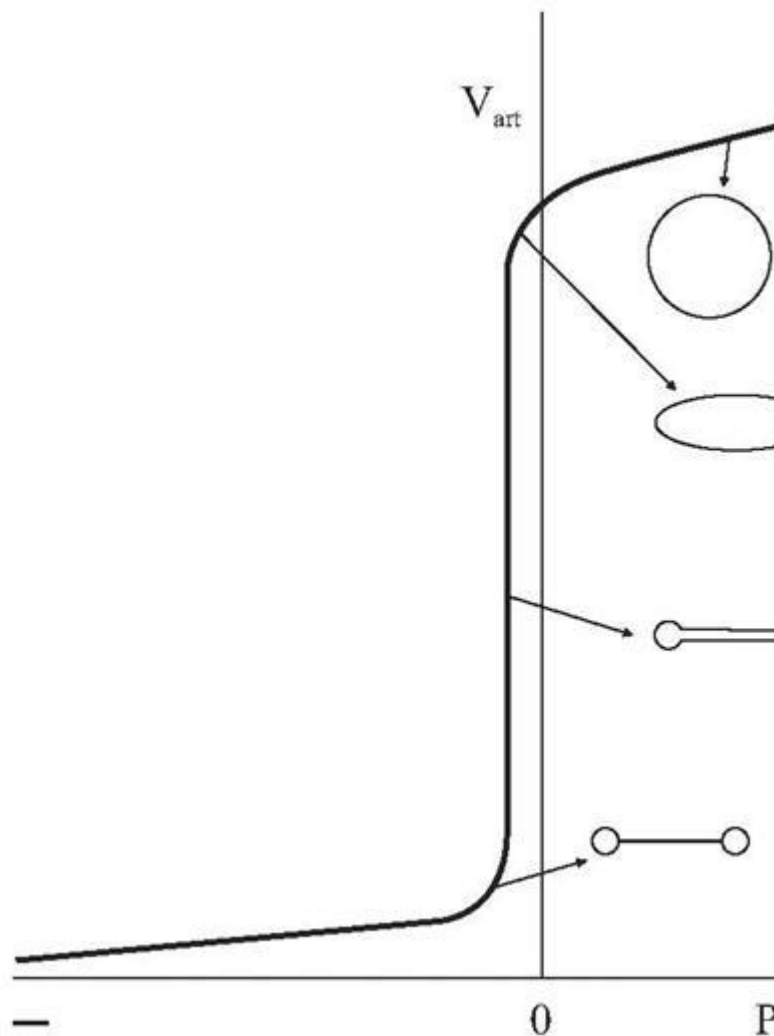
The transmural pressure – arterial volume under the cuff curve (see Figure 8.12) explains the amplitude changes of oscillometric pulses. Change in arterial volume changes the cuff volume, and so the cuff pressure. Based on the measured cuff pressure changes (oscillations) arterial volume changes can be calculated.

Figure 8.12. Principle of oscillometric blood pressure measurement



The right subfigure of Figure 8.12. shows the oscillometric amplitudes as a function of cuff pressure. The oscillometric method basically determines the arterial mean pressure. When cuff pressure equals to arterial mean pressure then the oscillometric amplitude is maximal. The classical method calculates the systolic and diastolic pressures from the mean pressure based on the oscillometric amplitudes. The systolic pressure equals to the cuff pressure that is higher than the mean pressure and the oscillometric amplitude corresponding to this cuff pressure is k_1 times the maximum amplitude. The diastolic pressure equals to the cuff pressure that is lower than the mean pressure and the oscillometric amplitude corresponding to this cuff pressure is k_2 times the maximum amplitude. The typical values are: $k_1 = 0.4 \dots 0.6$; $k_2 = 0.7 \dots 0.9$.

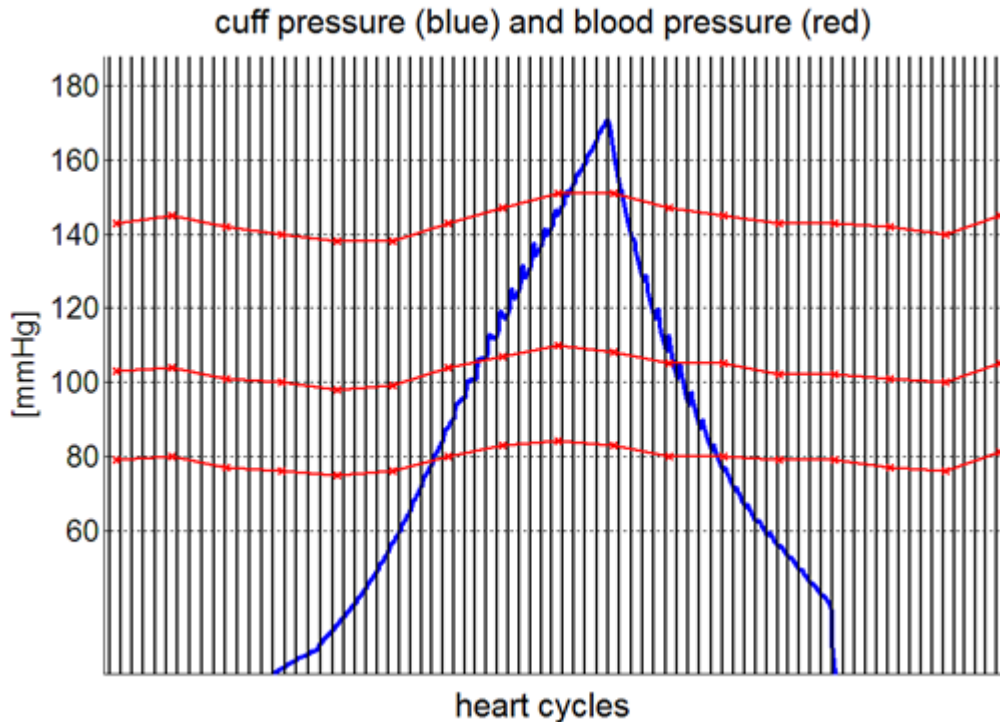
Figure 8.13. The cross section of the artery changes as cuff pressure increases



The modern oscillometric blood pressure meters take into account further parameters beside oscillometric amplitudes.

The steepness of the oscillometric pulse is such a parameter. It is supposed to be maximal when cuff pressure equals arterial mean pressure.

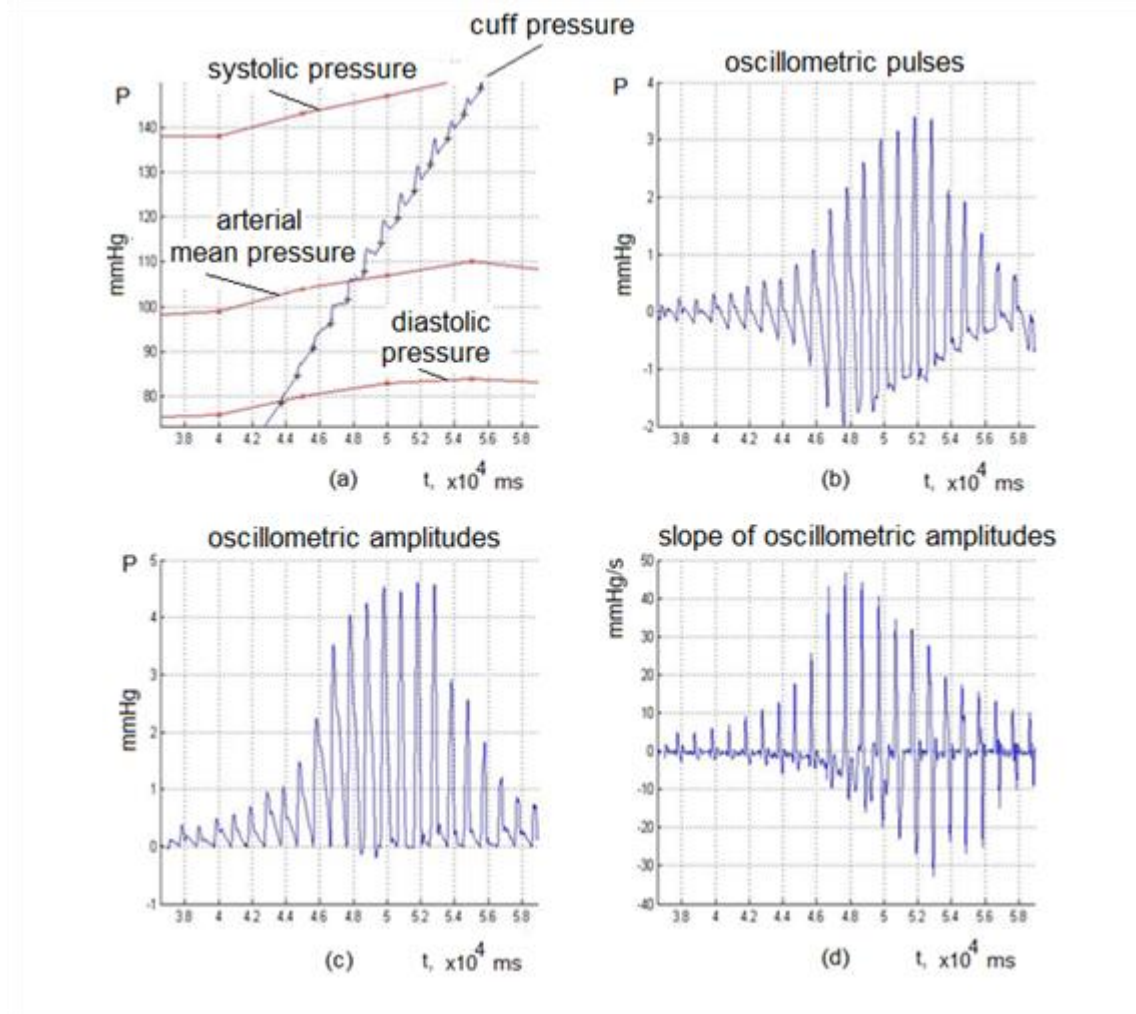
Figure 8.14. The result of invasive and cuff based blood pressure measurement taken in parallel. Red curves show the systolic, mean and diastolic pressures measured invasively. The cuff pressure of the indirect measurement is in blue.



The oscillometric pulses in the cuff pressure during both inflation and deflation can be seen in Figure 8.14. Inflation was slow (6 mmHg/s). The blood pressure of a patient in a post-operative ward was measured with a cuff based non-invasive device in parallel with invasive monitoring. The cuff was placed around the upper arm (cuff pressure vs. time function is blue), the non-invasive sensor was in the femoral artery (systolic-, diastolic- and mean pressure vs. time functions are red). For this patient the systolic-, diastolic- and mean pressures increased during the inflation, and decreased during the deflation of the cuff. Figure 8.15 shows the inflation phase in detail: (a) the cuff pressure and the systolic-, diastolic- and mean pressures measured invasively; (b) the oscillometric pulses; (c) the oscillometric amplitudes; (d) the steepness of the oscillometric amplitudes. The oscillometric amplitude is calculated from the oscillometric pulse. It is the difference of the peak value and the starting value marked by + sign in (a). In (a) the arterial mean pressure measured invasively is 107 mmHg (at 4.8×10^4 ms it is equal to the cuff pressure). The oscillometric amplitude is maximal four heart cycles later; based on (b) and (c) is at 5.2×10^4 ms. In turn, the steepness of the oscillometric pulse is maximal at 4.8×10^4 ms. Figures 8.14 and 8.15 illustrate that *the maximal oscillometric amplitude is not always at that cuff pressure which is equal to arterial mean pressure!* We also cannot conclude that arterial mean pressure is equal to the cuff pressure when the steepness of the oscillometric pulse is maximal. Different algorithms are incorporated into blood pressure monitors available on the market. At the web page www.mit.bme.hu/bpm there are several hundred records taken during cuff based indirect blood pressure measurements. The inflation of the cuff was slow (6 mmHg/s). The records can be analysed using Matlab. The details of the records together with an m-file reading the records into Matlab can also be found on the web page.

Non-invasive measurement of pressure-time function in the finger artery is possible also by applying the Peñáz method [8.18]. The pressure of the cuff around the finger is varied so that the transmural pressure of the artery is always around zero. In ideal case the cuff pressure is always equal to the pressure inside the artery. Infrared LED illuminates the finger and a phototransistor measures the light intensity attenuated by the blood in the artery. The cuff pressure is controlled so that the diameter of the artery – and so the attenuation – remain constant. This requires a fast pneumatic controller which is expensive. It is not easy to determine the unloaded artery diameter which must be kept constant. The haematocrit value and the smooth muscle tone influence the unloaded arterial diameter which must be determined from time to time (calibration).

Figure 8.15. The inflation phase of the measurement shown in Figure 8.14. (a) cuff pressure (blue) and invasively measured pressures (red), (b) oscillometric pulses, (c) oscillometric amplitudes, (d) steepness of oscillometric pulses.



Cuffless continuous monitoring of blood pressure is in the research phase. The pulse wave velocity in the artery (PWV) depends also on systolic blood pressure as described by the Moens – Korteweg equation (see eq. 8.4).

$$PWV = \sqrt{\frac{Eh}{\rho d}} \quad (8.4)$$

where E is Young's modulus of arterial wall corresponding to BP0 systolic pressure, ρ is the density of blood, d is the inner diameter of the artery. Monitoring ECG and the photoplethysmographic signal on the fingertip the pulse wave propagation time (ΔT_{EP}) can be determined. The stroke volume is ejected (and thus pulse wave starts) at the end of the isovolumetric contraction of the left ventricle (S point of ECG). QRS peak is easily detectable but the end of the isovolumetric contraction cannot be measured non-invasively. The method is applicable for the monitoring of *changes* in systolic pressure, thus the duration of isovolumetric contraction is supposed to be constant (a good estimate is 50 ms). The positive slope of the PPG (reflexive method) marks the arrival of the pulse wave to the fingertip (see chapter 4.2.2). PWV can be calculated if the left ventricle – fingertip distance (L) is known, see eq. 8.5.

$$PWV = \frac{L}{\Delta T_{EP}} \quad (8.5)$$

Figure 8.16 shows ΔT_{EP} during slow inflation and deflation of the cuff. The modulation effect of breathing can be significantly reduced if PPG is measured on both index fingertips and ΔT_{EP} of the right arm is subtracted from ΔT_{EP} of the left arm (provided the cuff is on the left arm). It is clear that inflation of the cuff increases ΔT_{EP} . To the same cuff pressure during inflation and deflation different ΔT_{EP} values belong. The possible reason is that as a result of compression by the cuff the E_0 value changes. The measure of change characterises the state of the brachial arteries. The actual value of Young's modulus depends on the systolic pressure, see eq. 8.6.

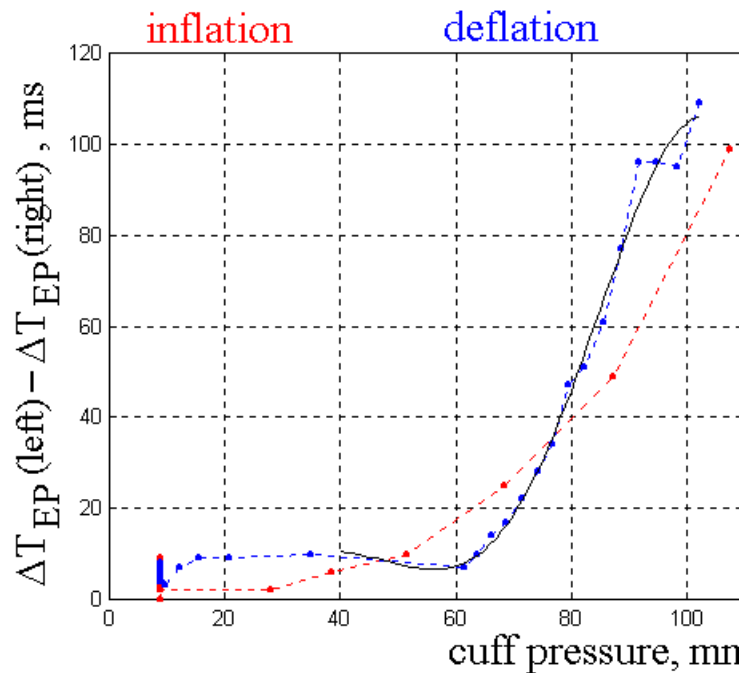
$$E = E_0 e^{aBP} \quad (8.6)$$

where a is a constant, BP is systolic pressure. BP is expressible, see eq. 8.7.

$$BP = \frac{1}{a} \left[\ln \left(\frac{L^2 \rho d}{E_0 h} \right) - 2 \ln(\Delta T_{PT}) \right] \quad (8.7)$$

The method requires frequent (in 5 – 10 minutes) recalibration [8.9].

Figure 8.16. The impact of inflation and deflation of the cuff on pulse wave propagation time



Sources of inaccuracy during blood pressure measurement

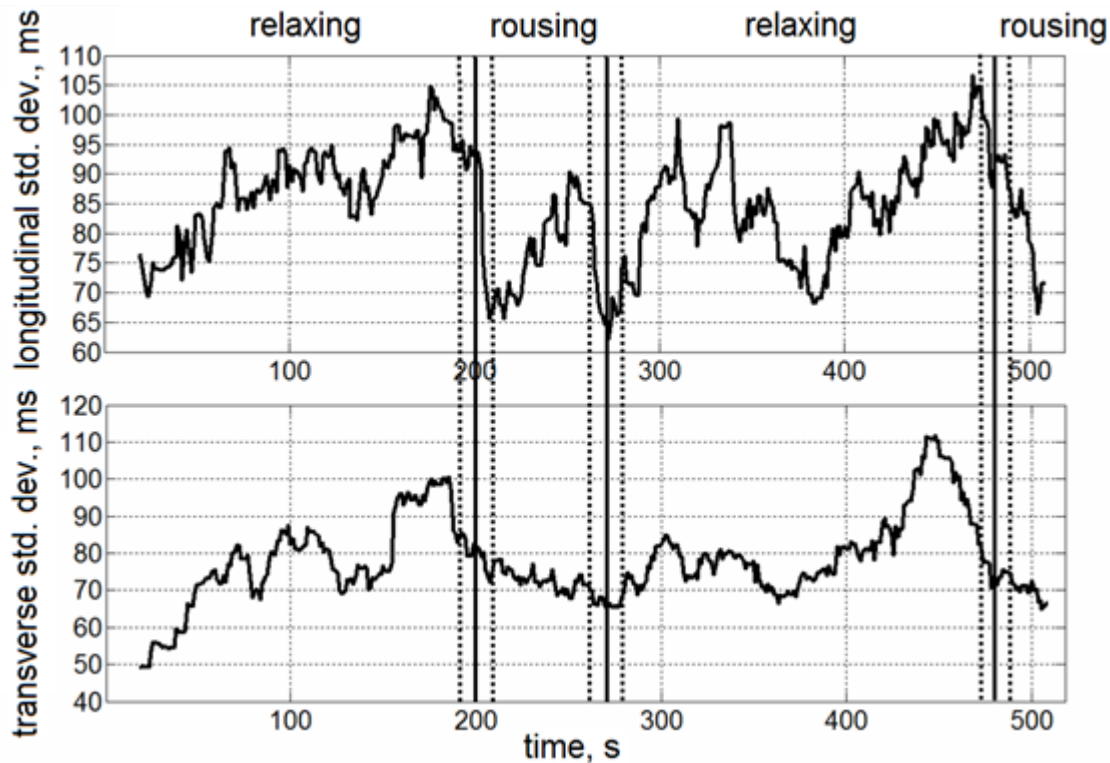
Characterisation of a person's blood pressure is rather difficult. It's not easy to answer the question: 'Is your blood pressure normal?' The answer by two numbers (e.g. 120/80 mmHg) is not sufficient. Blood pressure varies during the day; a momentary value is not necessarily typical for the person (see Figure 8.2 or the movie referred to in section 8.1). Physical or mental stress affects the blood pressure. To minimise this influence the person's stress level during blood pressure measurement should be kept low. The stress level should be checked before the measurement and if it is found to be high we have to wait until the person calms down. The stress level can be estimated based on the Poincaré plot of heart cycle times (see chapter 4.2.3). Figure 8.17 shows the stress level of a young healthy male while he was listening to different types of music. (The stress level is estimated by the transversal standard deviation of the Poincaré plot of tRR values.) There were two types of music; marked in Figure 8.17 as 'relaxing' and 'rousing' [8.23]. The person was sitting leisurely; the Poincaré plot and its longitudinal and transversal standard deviation were determined using the ECG taken in Einthoven I lead. Higher transversal standard deviation belongs to 'relaxing' than 'rousing' music. It is also apparent that change in standard deviation is delayed to change in music type. Stress level of a person can be characterised based on the Poincaré plot after personalisation: records have to be taken in known relaxed as well as in known stressed state.

Let's suppose we can determine the systolic and the diastolic blood pressure of a person belonging to a heart cycle. This does not guarantee that these values are typical for the person! The blood pressure might have changed as a result of the measurement, e.g. by the occlusion of the artery.

In case of cuff based indirect measurements sclerotic artery distorts the result: blood can flow even if cuff pressure is higher than systolic pressure. The rigid arterial wall cannot be bent with small radius, see lowest cross section in Figure 8.13.

The cuff size must be selected according to the upper arm. There are three main cuff sizes for adults (the circumference of the upper arm is given in brackets): small, 10 x 24 cm (22 – 26 cm), normal, 13 x 30 cm (27 – 34 cm) and big, 16 x 38 (35 – 44 cm). Improper size cuff can distort the measurement by 10 – 15 mmHg.

Figure 8.17. Assessment of stress level based on the transverse standard deviation of the Poincaré plot



Cuff must be placed tightly in the proper direction (this is marked on the cuff unambiguously). Cuff placed loosely or upside down can cause 10 – 15 mmHg error. Figure 8.18 shows a recording taken with a cuff placed around the sleeve of a shirt. Cuff pressure is in blue; PPG recorded on the left index fingertip (cuff was on the left upper arm). The tested young healthy male's blood pressure was measured ten minutes earlier with a properly placed cuff and the result was 115/80 mmHg. It is clear that the amplitude of the PPG only slightly decreases during inflation. The pulsation in the PPG is present when the cuff pressure is around 150 mmHg, well above the likely systolic pressure. As a result, the oscillometric blood pressure meter overestimated the systolic pressure.

Figure 8.18. The impact of placing the cuff on a shirt sleeve

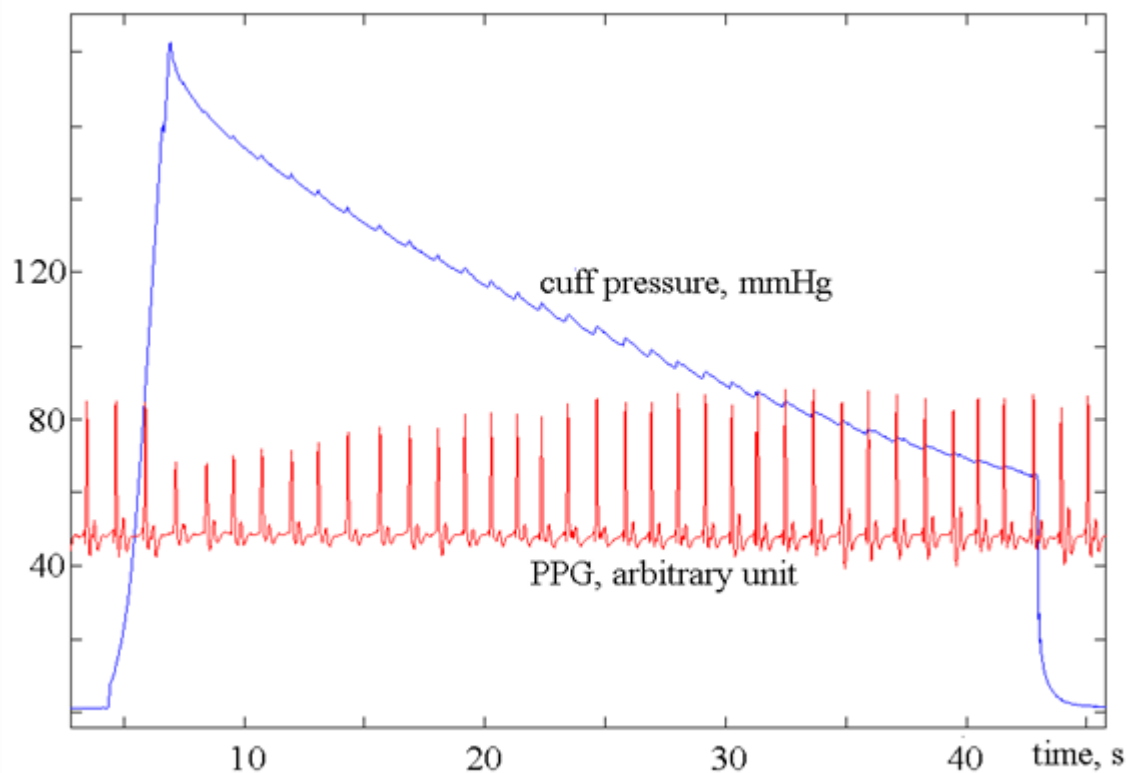
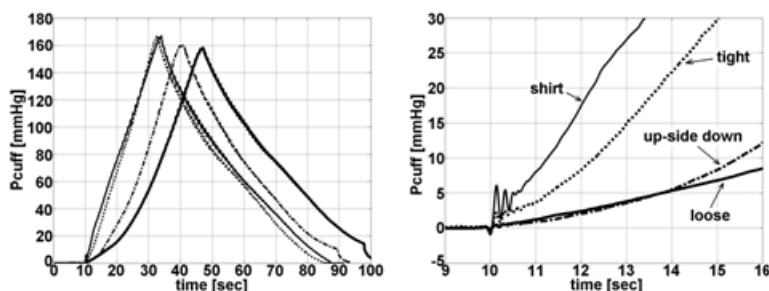


Figure 8.19. Cuff placement (tight, loose, upside down and on a shirt sleeve) can be identified at the beginning of slow inflation [8.24]

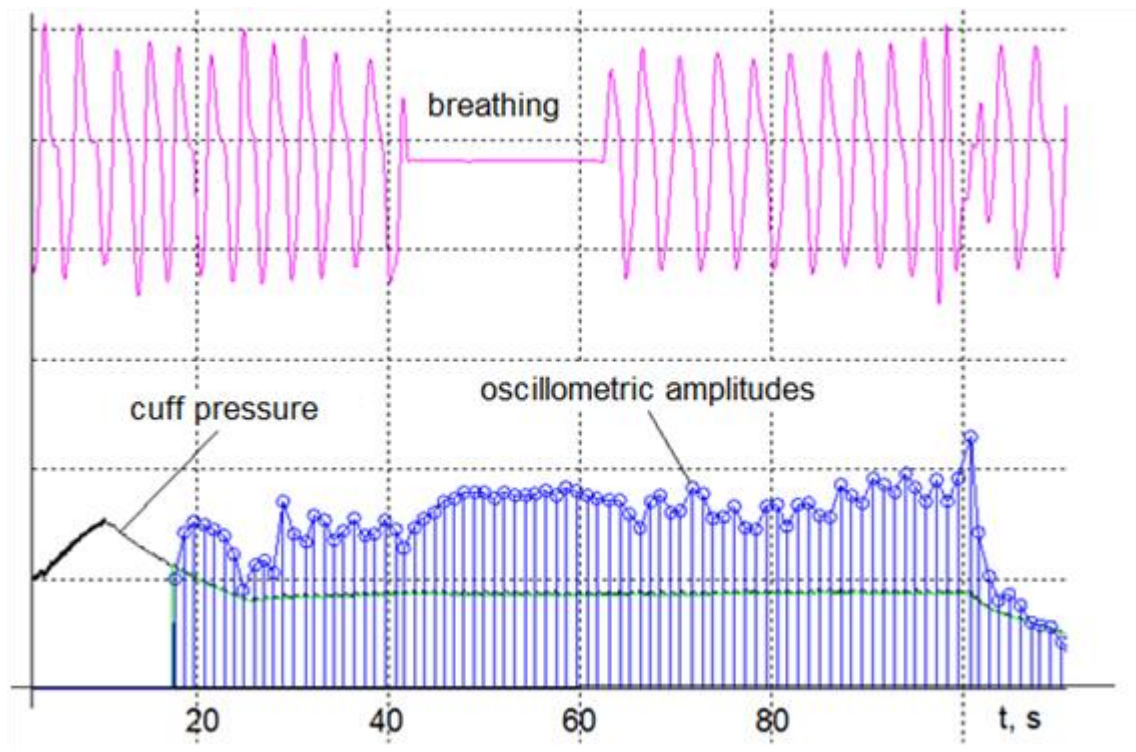


Cuff placement (tight, loose, upside down and on a shirt sleeve) can be identified by evaluating the early phase of slow inflation (see Figure 8.19) [8.24]. Early detection is advantageous because inflation can be stopped if necessary before the artery is occluded and so there is no need to wait at least five minutes for the next measurement (while the effect of occlusion passes away).

Arrhythmic heart cycle changes the oscillometric amplitude substantially. Most algorithms disregard oscillometric pulses belonging to arrhythmic heart cycles because no proper compensation algorithm has been found yet (what would have been the amplitude if the heart had contracted in time).

Breathing influences oscillometric amplitudes (see Figure 8.20). The upper subfigure shows air flow vs. time, the lower subfigure shows oscillometric amplitude vs. time in blue and cuff pressure vs. time in black. The cuff pressure was held constant between the 25 – 70 s interval. The tested person (young healthy male) held his breath for 20 s. During this interval (40 – 60 s) – after a short settling time – the oscillometric amplitudes are nearly constant. During breathing the intrathoracic pressure changes. As a result, momentary blood pressure might change: decrease during inspiration and increase during expiration. This influence is person specific.

Figure 8.20. Breathing influences the oscillometric amplitude values



The accuracy of blood pressure meters cannot be easily defined and determined because persons with etalon blood pressure do not exist. There are testers (simulators) that can be attached to blood pressure meters in place of the cuff. These testers produce different pressure-time functions. Manufacturers test their blood pressure meters using such simulators.

According to both the British and the American standard the best qualification is given to a blood pressure meter that has a deviation higher than 10 mmHg in 15% of the measurements. (The reference value is determined by a medical expert with auscultation and palpation in parallel with the tested meter.) 5 mmHg systematic error could cause improper treatment of 50 million Americans! If the 5 mmHg systematic error of all blood pressure measurements were negative then many would not get antihypertensive medication although they would need it. If the 5 mmHg systematic error were positive then many would get antihypertensive medication unnecessarily [8.19].

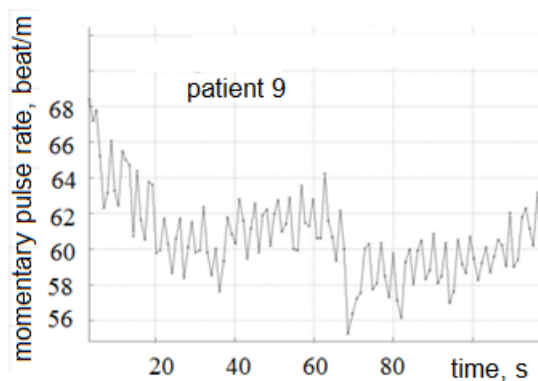
Figure 8.21. HHMD, a device for home health monitoring

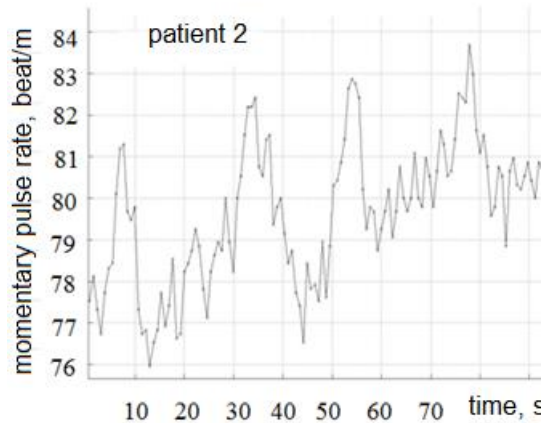


Research work is going on to personalise blood pressure measurement, i.e. an optimal evaluation algorithm for each tested person. This will allow a more accurate assessment than present day algorithms that have to calculate the blood pressure values of persons with cardiovascular systems in very different state. The optimisation process might need the measurement of other parameters. When the personalisation is over the measurement process is not longer than it is today.

Figure 8.21 shows a device for home health monitoring (HHMD, see section 4.2.1). It measures cuff pressure, ECG in Einthoven I. lead, PPG on the left and right index finger using infrared and red light. The two palms have to be placed on the disk shaped ECG electrodes so that the index fingertips are on the PPG sensors. The second electrode under the right hand serves for body potential driving (see section 3.2.3). Based on the PPG measurement using two wavelengths oxygen saturation of blood can be calculated. Figure 8.22 shows the momentary pulse rate of tested patients calculated from the ECG. This parameter is informative for the cardiologist. The pulse rate of both patients varied substantially but differently during blood pressure measurement with HHMD.

Figure 8.22. Momentary pulse rate changes during cuff based blood pressure measurement. The two patients' pulse rate varied substantially but quite differently



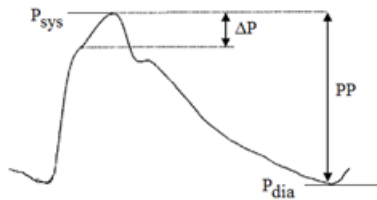


The elasticity of vessel walls can be characterised by the augmentation index, see Figure 8.23. This index expresses the pressure rising as a result of reflections in the blood vessels. Standard measurement and evaluation process is not available although research work is going on in several laboratories. The usual definition of the augmentation index is given in eq. 8.8.

$$AIx(\%) = \frac{\Delta P}{PP} \quad (8.8)$$

where ΔP is the pressure rise from the early systolic peak pressure to systolic pressure, PP is pulse pressure, the difference of systolic and diastolic pressure.

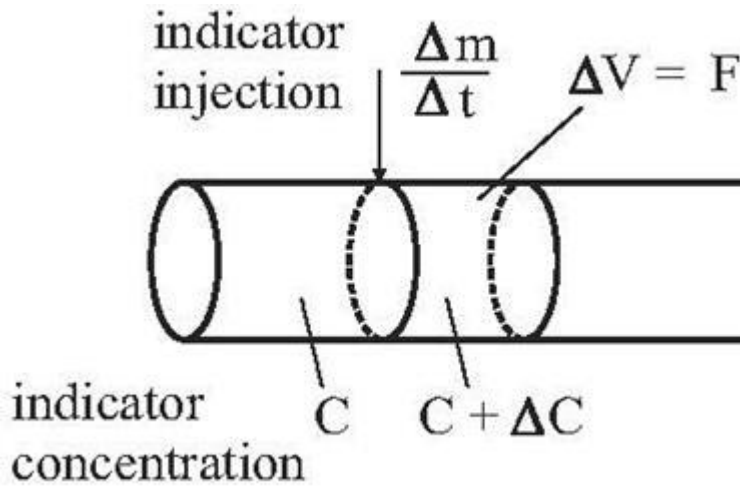
Figure 8.23. The aortic pressure vs. time function, the parameters necessary for the calculation of the augmentation index are marked (ΔP and PP)



4. Measuring blood flow and cardiac output

The concentration of oxygen and nutrients in the cells is informative for the medical doctor. It can be measured only invasively. An alternative solution is to measure blood flow that usually correlates with nutrient concentration. (It is even simpler to measure blood pressure which is related to blood flow.) Conventional flow sensors are not appropriate for the measurement of blood flow. The usually applied methods are based on dilution of an indicator, e.g. dye. Dilution based methods are unable to measure momentary values, they measure average flow. At a given point – within Δt interval – adding to the flowing blood Δm of the indicator its concentration increases by $\Delta C = \Delta m / \Delta V$. ΔV is the volume that passes along the injection point during Δt time (see Figure 8.24). $\Delta V = F \Delta t$, where F is the volume flow, its dimension is volume/time; in case of blood flow litre/minute. If the blood flow at the injection point is continuous then the constant concentration difference can be sustained by constant indicator injection.

Figure 8.24. Measuring blood flow using indicator injection



The increase of concentration is:

$$\Delta C = \frac{\Delta m}{\Delta V} = \frac{\frac{\Delta m}{\Delta t} \Delta t}{\frac{\Delta V}{\Delta t} \Delta t} = \frac{\frac{\Delta m}{\Delta t}}{F} \quad (8.9)$$

Volume flow can be expressed:

$$F = \frac{\Delta V}{\Delta t} = \frac{\Delta m / \Delta t}{\Delta C} \quad (8.10)$$

This procedure can be used to measure cardiac output. Cardiac output is the volume of blood pumped by either ventricle of the heart in one minute. Provided we can measure the oxygen consumption ($\Delta m / \Delta t$, litre/minute), the oxygen concentration of the arterial (C_a , litre/litre) and venous (C_v , litre/litre) blood then the volume flow of blood (F , litre/minute) can be determined, see eq. 8.11.

$$F = \frac{\Delta m / \Delta t}{C_a - C_v} \quad (8.11)$$

The method based on oxygen concentration measurement is called Fick's method. The concentration of venous blood returning via superior and inferior vena cava and via the coronary veins is different. The contraction of the right ventricle mixes the venous blood. A true mixed venous sample can be drawn from the tip of the pulmonary artery. For the oxygen consumption measurement the person inhales 100% oxygen, thus the inspired volume equals to the volume of the inspired gas. In the expired gas the oxygen concentration is measured so the oxygen consumption can be calculated. The disadvantage of the method is that it requires invasive intervention.

Typical values for a healthy male are: arterial O₂ concentration 200 ml/l, venous O₂ concentration 150 ml/l, O₂ consumption 280 ml/min; cardiac output 5.6 l/min.

Other indicators (e.g. dye) can also be used. Heating or cooling of blood and measuring the temperature is another possible method, see eq. 8.12.

$$F = \frac{q}{\rho_v c_v \Delta T} \quad (8.12)$$

where F is volume flow of blood (litre/minute), q is the heat transferred to blood over unit of time (W) c_v is the specific heat of blood (J/[kg K°]) and ΔT is the temperature difference caused by heating.

Indicator can be added to blood by applying a single injection. In practice it can be performed easier. Within a ΔV volume of the arterial circulation the concentration of the indicator $C(t)$ changes in time depending on the amount of indicator (Δm) actually in ΔV , see eq. 8.13. Figure 8.25 shows the concentration of the indicator in ΔV as a function of time.

$$C(t) = \frac{\Delta m}{\Delta V} = \frac{\Delta m}{F \Delta t} \quad (8.13)$$

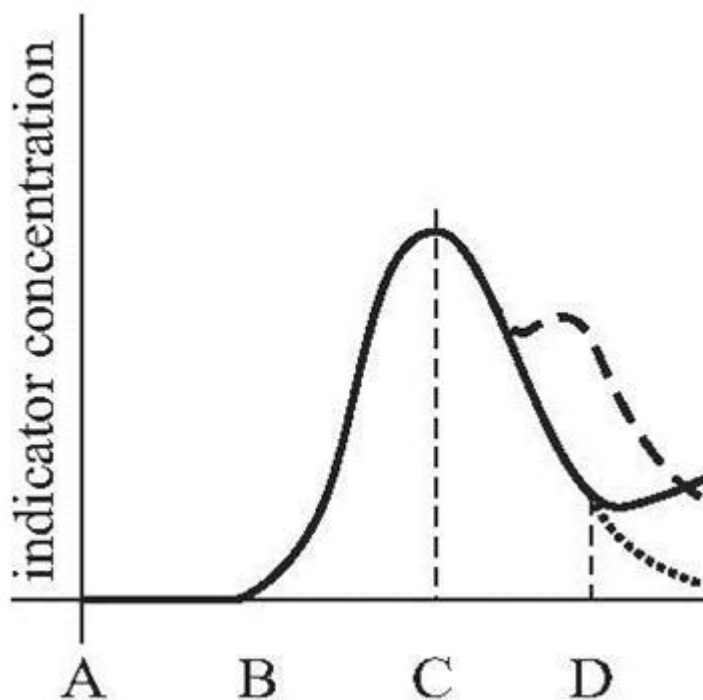
$$\Delta m = FC(t)\Delta t \quad (8.14)$$

$$m = \int_0^{t_1} FC(t)dt \quad (8.15)$$

If F is constant, then

$$F = \frac{m}{\int_0^{t_1} C(t)dt} \quad (8.16)$$

Figure 8.25. Measuring blood flow by single indicator injection based on concentration vs. time function



Following the injection of the indicator (A) the concentration at the observation point starts increasing (B). Having reached the maximum value (C) the concentration drops exponentially. In an open system the concentration would drop to zero as shown with the dotted line (E). At time D the concentration starts increasing again because the blood circulation brings back the indicator to the observation point again. The dashed line is valid for a patient with congenital heart defect i.e. with a hole in the septum between the left and right side of the heart. This results in the mixing of oxygen-rich blood with oxygen-poor one. Indicator can be dye or cooled saline solution.

Measurement of blood flow can be done using ultrasound sensors, see Figure 8.26. A and B are ultrasound transmitters.

Figure 8.26. Measuring blood flow with ultrasound sensors



As a result of blood flow the ultrasound gets faster from A to B than from B to A.

$$t_{AB} = \frac{d}{v_{UH} + v_{blood} \cos \alpha}, \quad t_{BA} = \frac{d}{v_{UH} - v_{blood} \cos \alpha} \quad (8.17)$$

$$t_{BA} - t_{AB} = \frac{dv_{UH} + dv_{blood} \cos \alpha - dv_{UH} + dv_{blood} \cos \alpha}{v_{UH}^2 - (v_{blood} \cos \alpha)^2} \quad (8.18)$$

Compared to v_{UH}^2 we can neglect $(v_{blood} \cos \alpha)^2$. (The difference is 5 – 6 orders of magnitude.)

$$\Delta t = t_{BA} - t_{AB} \cong \frac{2dv_{blood} \cos \alpha}{v_{UH}^2}, \quad v_{blood} \cong \frac{v_{UH}^2 \Delta t}{2d \cos \alpha} \quad (8.19)$$

The method can be applied using transmitters on the same side of the vessel. This requires a reflecting plate on the other side, see Figure 8.27.

Figure 8.27. Measuring blood flow with ultrasound sensor on the same side of the vessel



Doppler ultrasound blood flow measurement detects the frequency shift caused by the moving formed elements (see Figure 8.28).

$$\Delta f \approx \frac{2f_{UH} \cos \alpha}{v_{UH}} v_{blood} \quad (8.20)$$

If $f_{UH} = 1 \text{ MHz}$, $v_{blood} = 1,5 \text{ m/s}$ and $\alpha = 45^\circ$, then $\Delta f = 1415 \text{ Hz}$.

Figure 8.28. Measuring blood flow based on the frequency shift caused by moving formed elements



Microcirculation can be assessed using laser-Doppler flow measurement [8.20]. The laser beam scatters on the flowing formed elements and the frequency of the beams shifts according to the velocity of the elements. Microcirculation can be characterised based on the frequency of the scattered and the reflected beams.

Figure 8.29. Measuring blood flow with electromagnetic sensor



Figure 8.29 shows the measurement of blood flow using electromagnetic sensor [8.20]. Fluid containing charged particles generates electrical field when it flows in magnetic field. The method is able to measure momentary – not only average – value of flow. In ideal case, supposing uniform magnetic field and uniform velocity profile – the output voltage of the sensor is given in eq. 8.21.

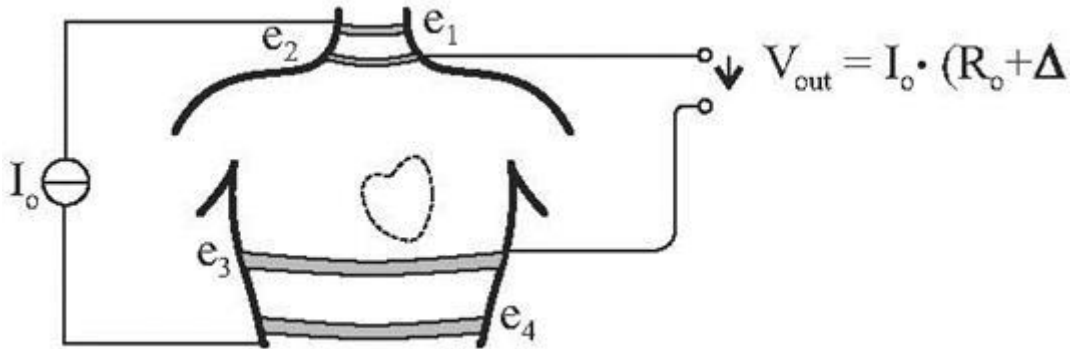
$$V_{out} = \int_0^L v_{blood} \times B dL \cong v_{blood} BL \quad (8.21)$$

where B is the magnetic field strength and L is the distance between the two electrodes measuring voltage. The sensor must encircle the vessel without deforming it. The position of the sensor relative to the vessel must remain constant during the measurement. This method is applied during surgical interventions.

Impedance cardiography (ICG) estimates the cardiac output noninvasively. In general, ICG assesses the parameters of blood flow in the thorax. The method is based on the fact that arterial blood ejected by the left ventricle changes the impedance of the thorax. By measuring the impedance we can estimate the ejected blood volume. Figure 8.30 shows the method supposing four stripe electrodes for impedance measurement. Based on comparative studies, results taken with point electrodes can be converted as if they had been measured using

stripe electrodes. Changes in cardiac output can be assessed by using point electrodes with the same resolution and accuracy as by using stripe electrodes.

Figure 8.30. The principle of measuring blood flow with impedance cardiography



There is a nearly constant arterial blood outflow from the thorax volume enclosed by the voltage measuring electrodes. Also, there is a nearly constant venous blood inflow into the same thorax volume. This must be taken into account during evaluation of measured data. The resistance of a thorax segment changes when its volume changes. If the distance is large enough between the current leading and voltage sensing electrodes then uniform current distribution can be assumed in the tested biological sample (in Figure 8.30 between electrodes e_2 and e_3). Considering the impedance real, an L long vessel with constant cross section area A filled with ρ resistivity blood has a resistance: $R = \rho L/A$. For further calculation the resultant resistance of vessels and tissue are considered to be connected in parallel, see Figure 8.31. (a). The resistivity of blood flowing in the vessels is smaller than the resistivity of tissues. As a result, the blood ejected to the arteries from the left ventricle decreases the resistance between e_2 and e_3 . Modelling the vessels with a cylinder shaped conductor, its cross sectional area and thus its volume (filled with blood) increases; see Figure 8.31. (b). The resultant resistance between e_2 and e_3 is the parallel resultant of the resistance of vessels and tissues (Figure 8.31. (a)). In a simple model the resultant of tissues is also supposed to have a cylindrical form. The cross sectional areas are A_{blood} and A_t . The resistance of the thorax R_{th} is the resultant of two parallel resistors (two cylindrical conductors).

Figure 8.31. The model used in impedance cardiography



$$\frac{1}{R_{\text{th}}} = \frac{A_t}{\rho_t L} + \frac{A_{\text{blood}}}{\rho_{\text{blood}} L} = \frac{V_t}{\rho_t L^2} + \frac{V_{\text{blood}}}{\rho_{\text{blood}} L^2} \quad (8.22)$$

$$V_{\text{blood}} = \frac{\rho_{\text{blood}} L^2}{R_{\text{th}}} - \frac{\rho_{\text{blood}}}{\rho_t} V_t \quad (8.23)$$

$$\Delta V_{\text{blood}} = \frac{\partial V_{\text{blood}}}{\partial R_t} \Delta R_{\text{th}} \quad (8.24)$$

$$\Delta V_{\text{blood}}(R_{\text{th}} = R_0) = -\rho_{\text{blood}} \left(\frac{L^2}{R_0^2} \right) \Delta R_{\text{th}} \quad (8.25)$$

where ρ_{blood} and ρ_t is the resistivity of blood and tissues, L is the distance between the voltage measuring electrodes, R_0 is the basic value of thorax resistance which can be measured at the end of diastole and ΔR_{th} is the change of R_{th} resulting from the ejection of the stroke volume. ΔR_{th} could be measured if there were neither arterial blood outflow nor venous blood inflow. Negative sign shows that arterial blood ejection decreases R_{th} .

ΔR_{th} cannot be measured directly because of blood in- and outflow. Figure 8.32 shows how we can estimate ΔR from the $R_{\text{th}}(t)$ function. Figure 8.32. (a) shows that following ventricular contraction the resistance of the thorax decreases until a minimum value and from that on increases until the next contraction. The minimum of the resistance must be estimated, what we would measure if there were no blood in- and outflow. Let's suppose that

following the minimum R_{th} increases at a constant rate. The rate of increase is projected back until the time instant when R_{th} started to decrease and we get the decrease in resistance ($\Delta R_{th}'$) that would be without blood in- and outflow. The decrease in resistance so estimated is given in eq. 8.26.

$$\Delta R_{th}' = T \left(\frac{\Delta R_{th}}{\Delta t} \right)_{min} \quad (8.26)$$

Based on it, the stroke volume is:

$$\Delta V = \frac{\rho_{blood} L^2}{R_0^2} T \left(\frac{\Delta R_{th}}{\Delta t} \right)_{min} \quad (8.27)$$

Figure 8.32. Evaluation of the thorax impedance vs. time signal recorded during ICG



Impedance cardiography does not give an accurate result for the stroke volume. The deviation from the actual value might be 15 – 20 %. In clinical practice monitoring the alteration is more important than the accuracy of the actual value. ICG is advantageous especially in intensive care units where it assures the non-invasive continuous monitoring of the cardiac output.

5. Problems

1. The cuff around the upper arm is by 13 cm higher than the left ventricle. Calculate the error it causes in blood pressure measurement.
2. We measure the blood flow according to Figure 8.26. The propagation velocity of ultrasound is $v_{US} = 1500$ m/s, the distance between the ultrasound transmitters is $d = 1$ cm, $\alpha = 45^\circ$ and $\Delta t = 10$ ns. Calculate the velocity of blood flow. Give the uncertainty of the measurement of blood flow velocity if the uncertainty of measuring Δt is 1 ns.
3. Convert the 120/80 mmHg to Pascal unit.
4. What are the three settings of the three-way stopcock in Figure 8.4 good for?
5. Why is it not sufficient to characterise blood pressure with two numbers?
6. What is the advantage of the oscillometric blood pressure measurement compared to the method based on Korotkoff sound detection?
7. How does breathing influence blood pressure?
8. What is the reason if blood flows even if the pressure of the upper arm cuff is higher than the systolic pressure?
9. Why is frequent calibration necessary using a cuffless blood pressure monitor that measures pulse wave velocity?
10. What is the reference during the calibration of automatic cuff based indirect blood pressure meters?
11. What kind of error can result from placing the cuff on the shirt sleeve?
12. How does the transversal standard deviation on the Poincaré plot of tRR values change when the stress level of the tested person increases?
13. Describe a method to measure cardiac output.
14. How does the impedance of the thorax change following ventricular contraction of the heart?
15. How accurately measures an ICG device cardiac output? Give an appropriate application of ICG.

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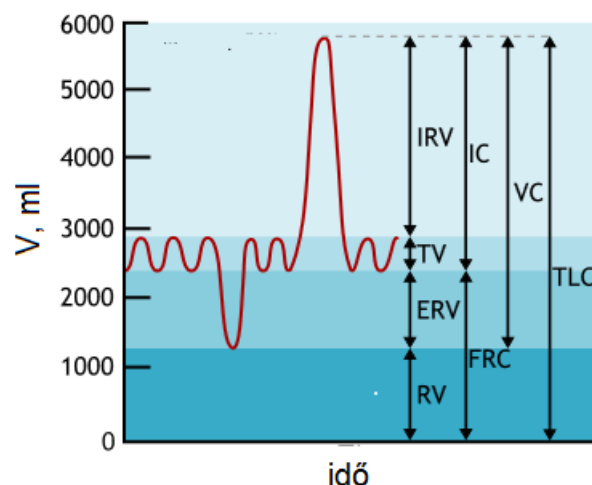
Chapter 9. Testing the respiratory system

Cells need to get oxygen and give up carbon dioxide. This is accomplished by the circulation and the respiratory system. The two systems are connected in the alveoli of the lungs. The lungs perform the so called external respiration and circulation performs the internal one. Pulmonary testers assess external respiration (breathing): air flow, inspired/expired volume, parameters of respiratory mechanics and the gas concentrations.

1. Measuring air flow and inspired/expired volume

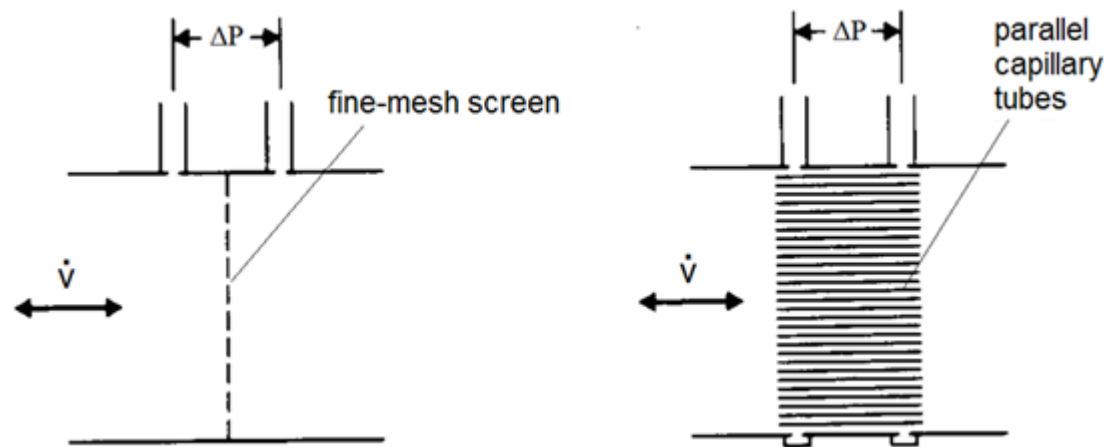
Figure 9.1 shows the change in lung volume during breathing. Following a few normal breaths, the tested person exhales as much air as possible. After another two normal breaths the tested person intakes maximum air into the lungs. The characteristic volumes are: TV (tidal volume, inspired/expired volume during one normal breath), IRV (inspiratory reserve volume), ERV (expiratory reserve volume), RV (reserve volume), IC (inspiratory capacity), FRC (functional reserve capacity), VC (vital capacity), TLC (total lung capacity).

Figure 9.1. The change of the lung volume during breathing (based on Wikimedia Commons, Lung Volumes And Capacities pl.svg.)



The measured parameter is air flow; inspired/expired volume is calculated by integration. There are two widely used flow sensor types: pneumotachometers and thermal convection flow meters. The scheme of a pneumotachometer, (like the Fleisch tube) is given in Figure 9.2.

Figure 9.2. The scheme of the Fleisch tube



The air flow across the resistance element produces pressure difference. The pressure difference – (laminar) air flow relationship is nearly linear, changes of the two quantities are in phase. The resistance is realised by applying a number of parallel capillary tubes with small diameter. These tubes can be realised by helically wound corrugated metal plate (see Figure 9.3). This layout assures laminar flow. Figure 9.4 shows the roll up of the corrugated metal plate. The resistance of a single tube is substantial but the many resistance (tube) in parallel give a small resultant. The resultant resistance must be small enough not to hinder breathing and big enough to produce easily measurable pressure difference. Considering the two contradictory expectations 1 cmH₂O resistance is a good compromise.

Figure 9.3. The resistance element of a Fleisch tube



Figure 9.4. The enlarged centre of the resistance element shown in Figure 9.3



The inner part of the Fleisch tube is usually heated up to 37 °C to avoid condensation. This reduces the risk of infection transfer between patients. Exchangeable bacterial- and viral filters are available; an example is Piston PBF 100 [9.1]. The resistance element can also be a fine-mesh screen, see Figure 9.5.

Pressure difference needs to be converted to electrical signal; differential capacitor is widely used for this purpose. Hybrid integrated circuit with voltage output signal is available with two mounted pipe ends. The pressure difference between the pipe ends moves the inner plate of a differential capacitor (see section 2.1.5) connected into a bridge circuit.

Figure 9.5. Flow resistance element realised by fine-mesh screen



The air flow – pressure difference transfer function is influenced by:

1. the non-linearity of the Fleisch-tube; $\Delta P = A\dot{V} + B\dot{V}^2$
2. the viscosity of the flowing gas.

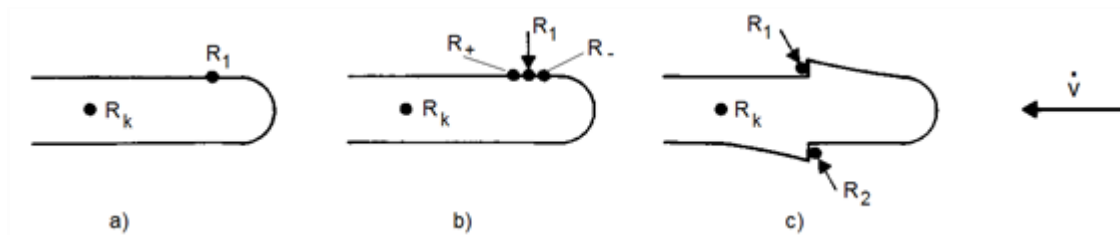
The A, B parameters of a given transducer can be determined by measurements. The identification requires the application of different air flow velocities known with high precision. The transducers can be calibrated even by the users. Manufacturers offer calibrating air pumps which are able to blast a given volume through the sensor in both directions. Calibration should be repeated a couple of times with different velocities being held as constant as possible (e.g. 1 l/s and 5 l/s).

The pressure difference at the output of the sensor is nearly proportional to the viscosity of the flowing gas. At 39 °C the viscosity of air is 183 µpoise, that of oxygen is 202 µpoise. This causes a 10% difference in output pressure difference between 100% oxygen and air flowing with the same velocity.

Integrating the air flow – time function we get the breathed volume – time function. It must be taken into account that the parameters of the exhaled air (at body temperature, 37 °C and saturated with water vapour) are different from the inhaled one (20 – 25 °C, humidity 40 ... 70 %). Furthermore, during inspiration the pressure in the lungs is lower while during expiration higher than in the room. The correction is called BTPS (body temperature and pressure, saturated).

The tap of the Fleisch tube closer to the mouth is used to connect to gas analyser and also to measure mouth pressure. Often there is an electronically controlled shutter in the Fleisch tube in between the two taps. When the shutter is closed then the pressure measured using the tap closer to the mouth is nearly equal to the pressure in the lungs.

Figure 9.6. Placement of thermistors in a thermal convection flow meter



The Fleisch tube has dead space. Part of the exhaled air remains in the tube it will be inhaled again.

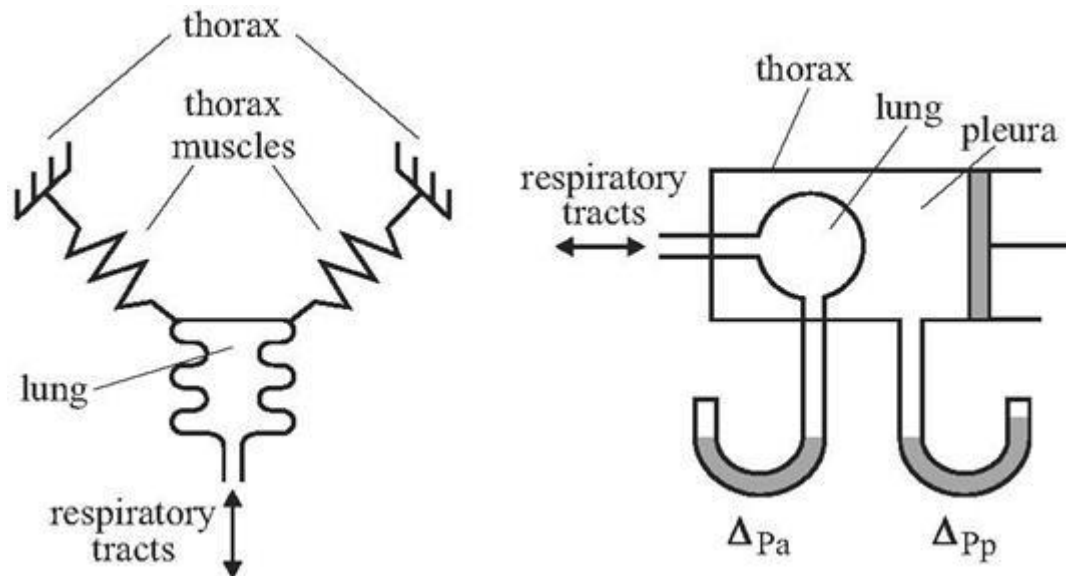
The thermal convection flow meter senses the cooling caused by the flow. Figure 9.6 shows the operating principle. The temperature drop of the heated element depends on the flow. The sensor should be calibrated by using the gas to be measured. The operation of the sensor in itself is independent of the flow direction. The inhaled and exhaled air flow can be separated and measured with two sensors. The high corner frequency of the sensor can reach 1 kHz. The dead space of the sensor is small; the applied thin wire hardly influences breathing.

R_1 is the heated thermistor; its resistance is kept at a constant value. Air flow cools the thermistor, keeping its resistance at a constant value requires a higher current. R_s senses the ambient temperature and it is not cooled by the air flow. In Figure 9.6 b) the R_+ and R_- ; in c) the R_1 and R_2 thermistors serve for detection of flow direction. Using compensating sensors the transfer function can be linearised. The disadvantage of the convection flow meters is their price.

2. Measuring parameters of respiratory mechanics

Figure 9.7 shows a possible model of respiratory mechanics.

Figure 9.7. A simple mechanical model of the lungs



Equation 9.1 describes the relation between volume change of the lungs and intrapleural pressure.

$$p_0 - p_p(t) = \frac{1}{C}V(t) + R\frac{dV(t)}{dt} + I\frac{d^2V(t)}{dt^2} \quad (9.1)$$

where C is compliance, R is resistance, I is inertance, p_0 is external pressure, p_p is intrapleural pressure. In medical practice compliance and resistance have diagnostic importance, inertance is rarely used. The resultant compliance of the lungs and thorax supposing small change in lung volume is estimated by the formula

$C \approx \frac{\Delta V}{\Delta p_p}$. The resistance of the airway is inversely proportional to its diameter. Many small diameter airways are connected in parallel so the resultant resistance is small. The section comprised of medium diameter airways

has the highest resultant resistance. Airways are widened by the volume increase of the lungs during inspiration; thus their resistance decreases. Breathing resistance is made up of airway resistance (R_a) and the resistance of lung tissues (R_t). Airway resistance (provided the lung volume is nearly constant) can be estimated by the

following formula: $R_a \approx \frac{P_0 - P_a}{\dot{v}}$. Airway resistance can be measured by activating the shutter in the Fleisch tube. Closing the shutter increases mouth pressure and decreases air flow (to zero). Based on it the airway

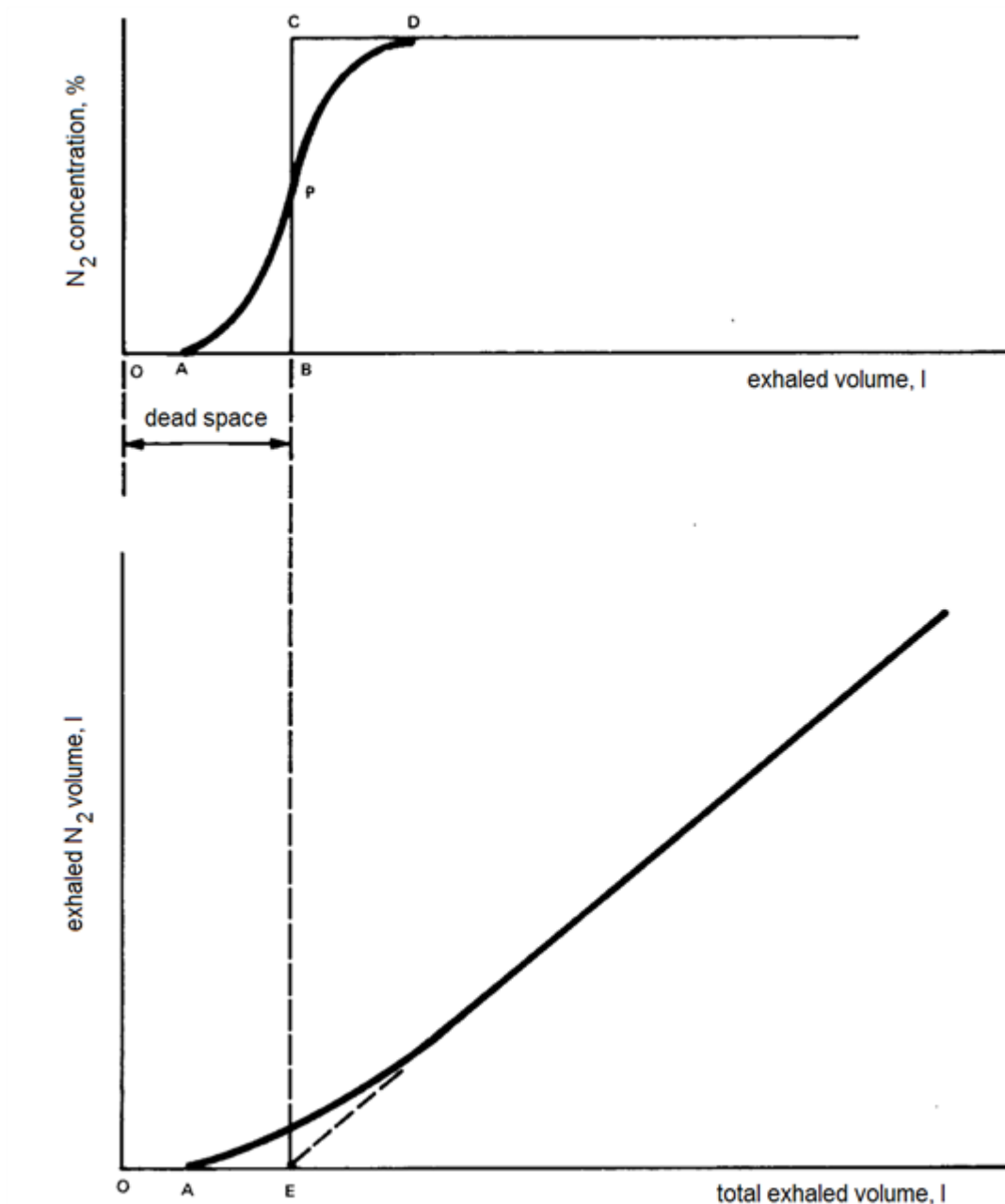
resistance can be estimated: $R_a \approx \frac{\Delta p}{\Delta \dot{v}}$. This method can be applied when the patient is sitting in a full body plethysmograph (see section 9.4).

3. Assessing gas exchange

Respiratory quotient is the rate of produced carbon dioxide and oxygen uptake: $RQ = \frac{V_{CO_2}}{V_{O_2}}$. It characterises the efficiency of breathing. There is pneumatic connection between the flow sensor and the gas analyser. Gas analysis requires the air to be transported to the analyser. This introduces a time delay between the volume of breathed air and the corresponding gas concentration. It must be compensated during processing. The delay time varies according to the suction of the analyser. Modern gas analysers can measure the actual delay time by processing the time functions of flow volume and gas concentrations. As an example, the $CO_2(t)$ function arises from nearly zero to 5 – 6% when expiration starts. The gas analyser must be fast enough to provide continuous concentration data. If this is available, the consumed oxygen can be calculated as given in eq. 9.2.

$$V_{O_2} = \int_0^{V_{in}} v(t) c_{O_2}(t) dV \quad (9.2)$$

Figure 9.8. Calculation of the dead space



For accurate gas analysis we need to know the total dead space. It has two components: anatomical (oral cavity and trachea) and technical (the dead space of the measuring equipment including tubes). Figure 9.8 shows the principle of measuring the total dead space. The patient inhales 100% oxygen. During the following expiration the N_2 concentration and the produced nitrogen is measured. Mixing of 100% oxygen and gases exhaled from the lungs takes place also in the dead space. We need to determine where would be the end of blowing out 100% oxygen (0% nitrogen) if there were no mixing. In Figure 9.8 this is at point P. P should be determined so that the ABP area is equal to DCP area. Similarly, using the curve showing the exhaled nitrogen volume as a function of total exhaled gas volume; the extension of the linear section points to total dead space (point E).

Alveolar ventilation can be measured with the help of neutral gas (most often nitrogen) not involved in gas exchange during breathing. By definition, it is the amount of air that reaches the alveoli and is available for gas exchange with the blood per unit time. Inspired gas distribution (IDI) is closely related to alveolar ventilation. Patients inhale 100% oxygen and the amount and the concentration of nitrogen in the exhaled gas are recorded. Total dead space must be known and taken into account in the calculation.

The drop of nitrogen concentration would be exponential if the lungs had a single compartment volume with ideal mixing of gases. Following the n^{th} expiration eq. 9.3 gives what the nitrogen concentration in the exhaled air would be.

$$c_n(N) = c_0(N) \left(\frac{FRC}{FRC + VA} \right)^n \approx c_0(N) e^{-\frac{nVA}{FRC}} \quad (9.3)$$

where FRC is functional reserve capacity, VA is the difference of tidal volume (TV) and the dead space. Keeping on with nitrogen washout until $c_n(N)$ equals 1% then we get eq. 9.4.

$$\ln[c_n(N)] = 0 = \ln[c_0(N)] - \frac{nVA}{FRC} \quad (9.4)$$

Let the nitrogen concentration at the beginning of the washout, $c_0(N)$ be 72%, we get eq. 9.5.

$$nVA = FRC \ln 72 \quad (9.5)$$

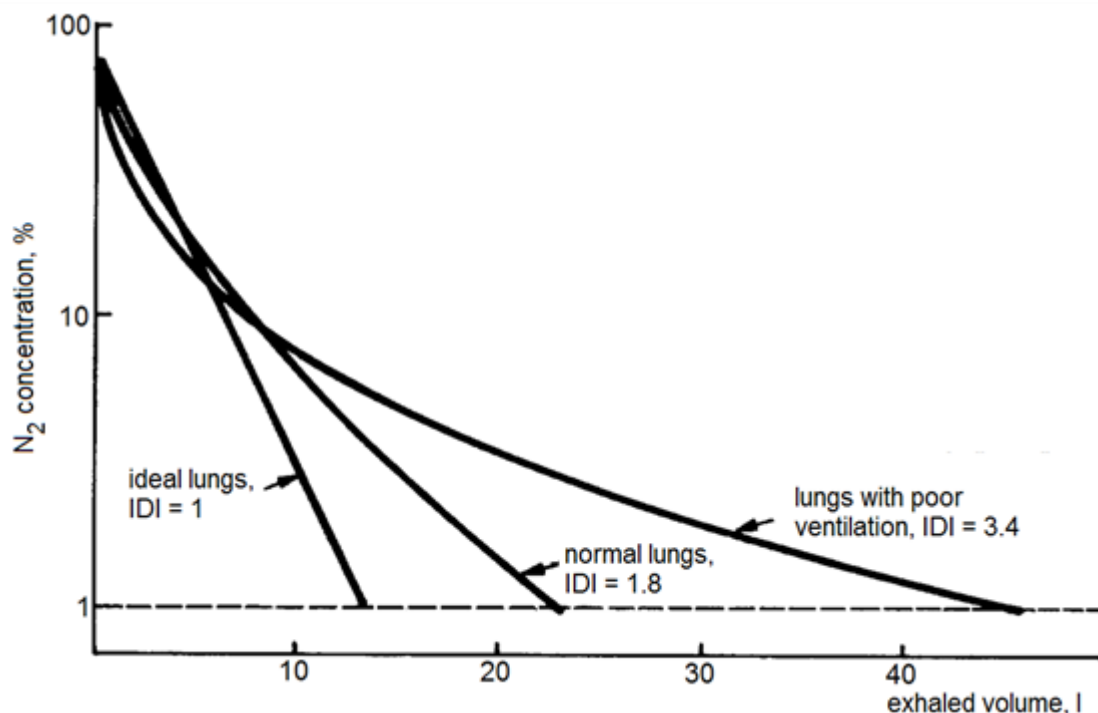
This means that $n \times VA$ exhaled air is needed to reduce the initial nitrogen concentration from 72% to 1%. The volume of lungs is divided into compartments and the mixing of gases is not ideal. As a result more exhaled air is needed to produce the drop in nitrogen concentration, see eq. 9.6.

$$IDI = \frac{nVA}{FRC \ln 72} \quad (9.6)$$

Figure 9.9 shows the drop in nitrogen concentration vs. exhaled air for ideal, one compartment lungs ($IDI=1$), for healthy subject ($IDI=1.8$) and for poor distribution ($IDI=3.4$). The mixing in the lungs is illustrated in Figure 9.10.

The functional reserve capacity (FRC) and reserve volume (RV) can also be measured using neutral gas not involved in gas exchange during breathing. One possible method is also nitrogen washout. Patient inhale 100% oxygen until the nitrogen concentration in their lungs drops to 1%. Prior to washout the initial nitrogen concentration is determined. Measuring the exhaled nitrogen volume, $FRC = (\text{exhaled nitrogen volume}) / (\text{initial nitrogen concentration})$. Dead space must be taken into account during calculation.

Figure 9.9. Measuring alveolar ventilation by nitrogen washout



During washout the usual nitrogen concentration in the lungs decreases. As a result nitrogen from the alveoli gets into the lungs. This distorts the above described measurement and explains why nitrogen concentration should not be decreased below 1%.

Following the inspiration of 100% oxygen a single expiration can also be assessed. Patients exhale until the volume of their lungs is minimal (RV) then inhale 100% oxygen. They slowly exhale until the volume of their lungs is minimal again (RV). Figure 9.11 shows typical results for the nitrogen concentration in the exhaled gas as a function of exhaled volume.

Phase I of the curve corresponds to the dead space, phase II shows the transition to alveolar gas. Phase III is called alveolar plateau, in it the oscillations are related to heart beats (as the heart presses the lungs). In ideal case (lungs with a single compartment and ideal mixing) in phase II the nitrogen concentration would be constant, the slope of the curve would be zero. Good mixing in the lungs of healthy subjects results in a slope not higher than 2%/500 ml. The slope is measured between 750 and 1250 ml exhaled volume. Airway obstruction or poor mixing of gas result in a slope higher than 2%/500 ml. The slope for smokers is about twice as high as for non-smokers. Phase IV is the expiration of the closing volume (CV). In the closing volume the gradient of nitrogen concentration substantially increases. Recording the nitrogen concentration during a single expiration (following 100% oxygen inspiration) also helps the diagnosis of increase in airway resistance (stenosis).

Figure 9.10. Distribution of gases in the lungs at maximal expiration (RV is the volume of lungs), at maximal inspiration (TLC is the volume of lungs) inhaling air or 100% oxygen

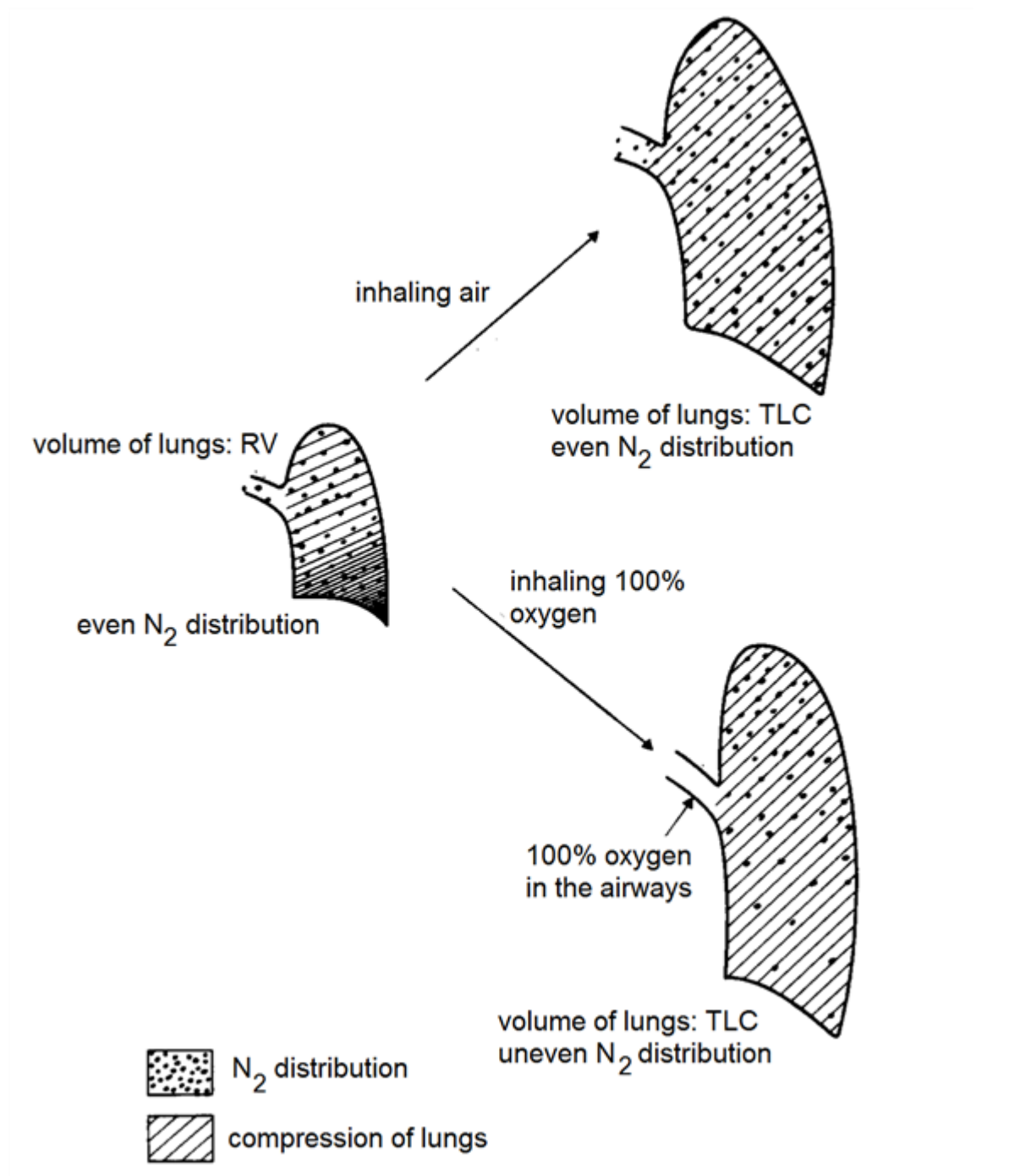
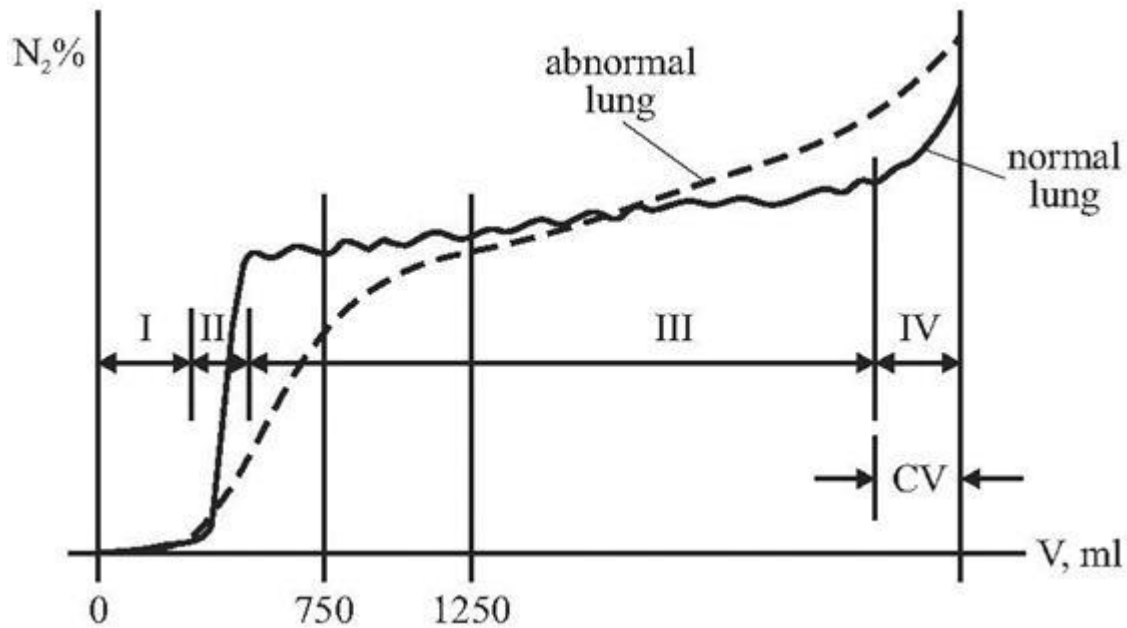


Figure 9.11. Nitrogen washout during a single expiration



4. Equipment

Qualitative assessment (mainly breaths per minute) of respiration is needed in intensive care unit equipment. This does not require the measurement of air flow. The impedance between two chest ECG electrodes measured at 50 – 100 kHz frequency drops during expiration and increases during inspiration. The measuring signal can be easily removed from the ECG by low-pass filtering.

Even the breathing of premature babies in an incubator can be monitored with a mattress with a number of compartments. There are airways between neighbouring compartments. Air is flowing through these airways when the pressure distribution changes as a result of breathing. Air flow in the airways can be detected easily.

Spirometers serve for the quantitative assessment of breathing. They can test three different breathing: normal-, forced breathing and hyperventilation. The diagnostic value of normal breathing is low. Its parameters can be easily modified by training.

The parameters of forced breathing are determined by anatomical build up; they cannot be influenced by practicing. (The measurement requires the cooperation of the tested person.) The typical values of healthy subjects were determined by statistical methods for homogeneous ethnic groups. These are called 'predicted values'; usually a normal value and the 80 – 120% range for each parameter. Three data determine the predicted values: age, height, gender. Comparing the measured forced breathing parameters to predicted values is done during screening tests. Figure 9.12 shows predicted values for FEV1 calculated according to different references [9.4]. Figure 9.13 shows the change of predicted values as a function of age.

Figure 9.12. Calculation of FEV1 based on different references
<http://www.spirxpert.com/GOLD.html> author: Quanjer PH)

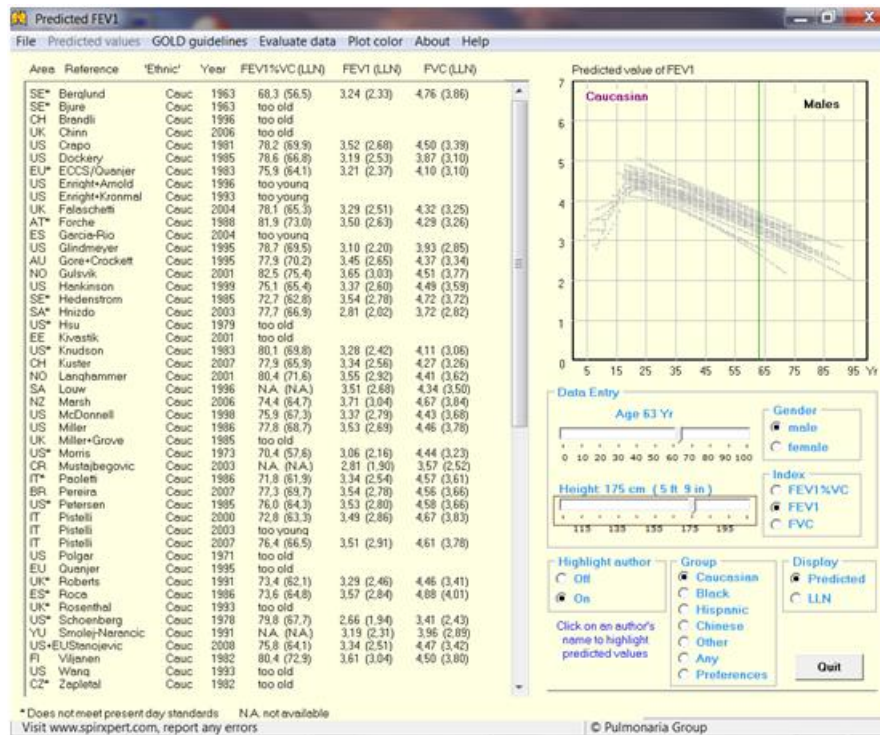
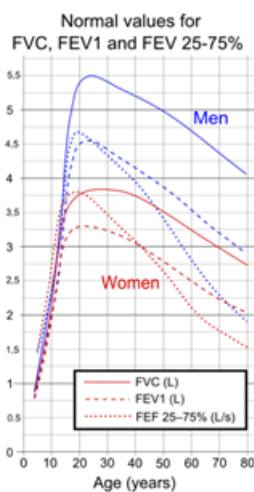


Figure 9.13. Predicted values of forced breathing change with age
http://commons.wikimedia.org/wiki/File:Normal_values_for_FVC,_FEV1_and_FEF_25-75.png author: Mikael Häggström)



The equation for European males [9.5]:

$FEV1 \text{ (litres)} = 4.301 \times (\text{height in meter}) - \text{age} \times 0.029 - 2.492$. A 22-year old male who is 180 cm tall should produce 4.6 litres FEV1. This predicted value drops to 4.4 l when he is 30 and to 3.8 l when he is 50 years old.

The predicted values were determined about 25 years ago, they should be updated [9.6].

Figure 9.14. Expired volume vs. time during forced expiration

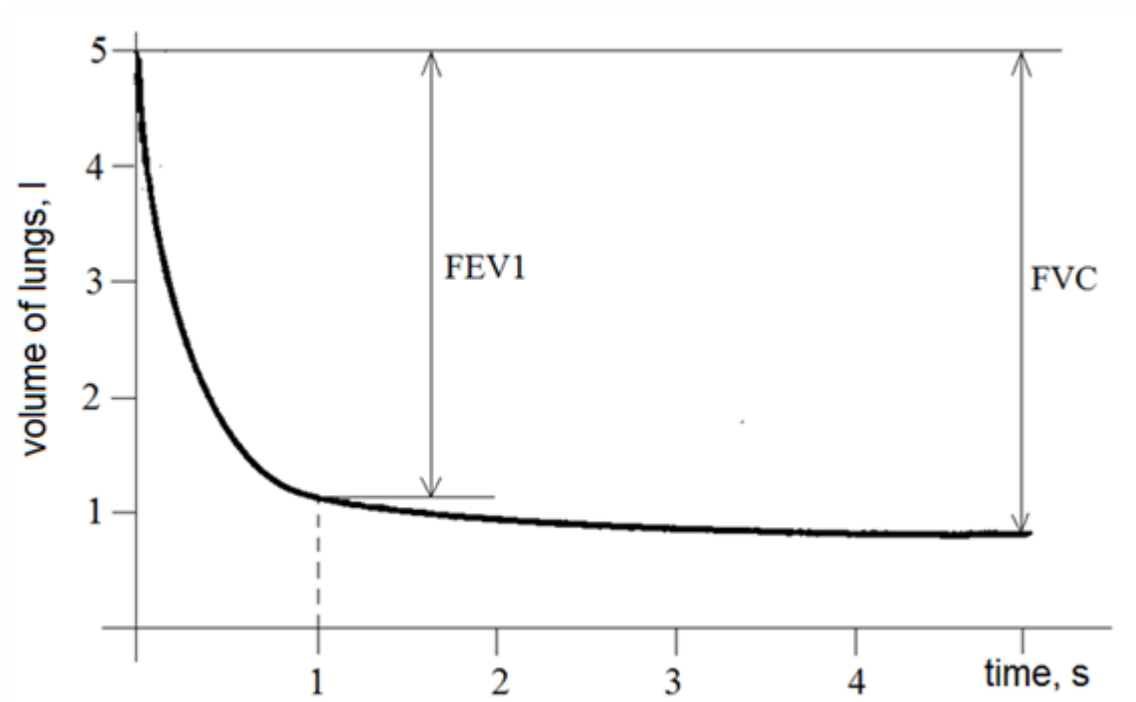
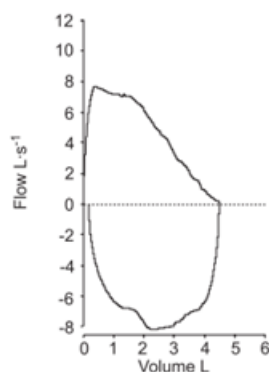


Figure 9.14 shows forced expiration volume vs. time function. The tested person inhales to maximum lung capacity (TLC) and then as fast as possible exhales to minimum lung volume (RV). The difference of the maximum and minimum lung volume is forced vital capacity: $FVC = TLC - RV$. Forced expiration is characterised by the expired volume in a given time. Within 2 seconds healthy subjects nearly reach RV; thus FEV1 and FEV2 (forced expiratory volume in 1 and 2 seconds) are important. Further significant parameter of forced expiration is the peak (or maximal) expiratory flow rate, PEFR (or MEFR). For healthy subjects the FEV1/FVC ratio is around 70%.

Persons are asked to repeat forced inspiration and expiration once or twice after a few minutes' break. The maximum values of all parameters (breathed volume, flow rate) are considered as characteristic for the person even if they were produced in different in- or expirations. Figures 9.15 – 9.18 show loop curves of flow rate vs. breathed volume for healthy subjects and patients. The result of a healthy male is shown in Figure 9.15. The maximum flow rate is around 8 l/s during both inspiration (PIFR, peak inspiratory flow rate) and expiration (PEFR, peak expiratory flow rate). The maximum flow rate is reached at the beginning of inspiration, while during expiration the maximum flow rate is reached when about half of FVC has been exhaled.

Figure 9.15. Flow rate – volume loop curve, healthy male



(Figures 9.15. – 9.18. are from: <http://www.thoracic.org/statements/resources/pfet/PFT2.pdf> authors Miller MR et al. [9.7].)

The maximum inspiratory flow rate of an asthmatic patient (see Figure 9.16) is reduced (about 6 l/s) the maximum expiratory flow rate is even smaller (about 4 l/s). The total inhaled – and so the total exhaled – volume is about the same as that of the healthy subject (about 4 l).

Figure 9.16. Flow rate – volume loop curve, asthmatic patient

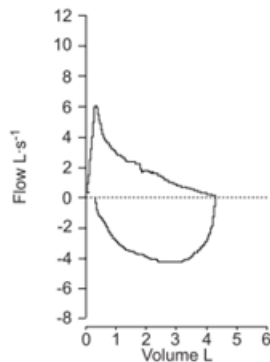


Figure 9.17 shows the loop curve of a patient with chronic obstructive pulmonary disease (COPD). The total inspired – and so the total expired – volume is about the half of what a healthy subject breathes (about 2 l). The maximal inspiratory and expiratory flow rates are about the same, 4 l/s. This is also about half of what a healthy subject produces.

Figure 9.17. Flow rate – volume loop curve, COPD patient

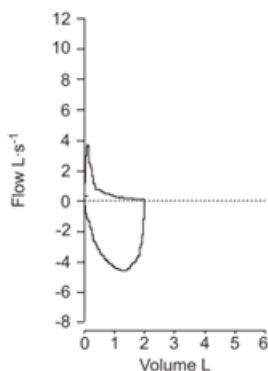
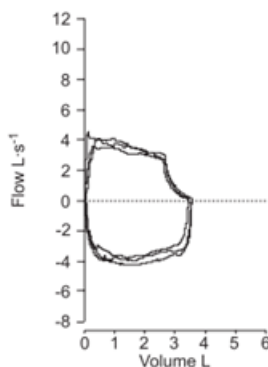


Figure 9.18 shows the loop curves of a patient with upper airway obstruction. The patient performed three forced breathing tests and produced very similar results.

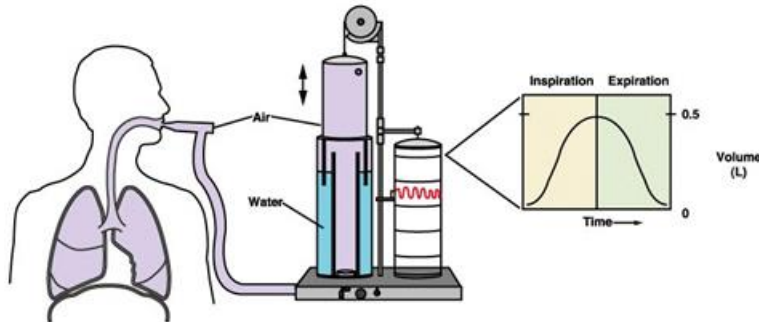
Figure 9.18. Flow rate – volume loop curve, patient with upper airway obstruction. The results of the three tests are nearly identical.



During hyperventilation tested subjects perform forced inspirations and expirations with the maximum possible frequency. As a result, both the oxygen concentration of blood and its pH value increase. Hyperventilation can be performed for 15 – 20 s. Longer hyperventilation would cause the blood pH value leave the normal range (7.30 – 7.45). This would lead to dizziness, even to blackout.

The breathing – time function does not have high frequency components, its spectrum is limited to a few Hz. The sampling frequency is usually 1 – 2 kHz mainly for accurate determination of the start of inspiration and for accurate gas analysis. Figure 9.19 shows the scheme of a classical spirometer using a bell.

Figure 9.19. Scheme of the classical spirometer using a bell (water seal spirometer)
<http://www.kmle.co.kr/search.php?Search=spirometer&SpecialSearch=HTMLWebHtdig&Page=10> Korean Medical Library Engine



The water sealed bell moves up and down during expiration and inspiration. A carbon dioxide filter is needed because tested persons inhale from the same volume to where they exhale. Sodium based filter can be used.

Figure 9.20 shows a whole body plethysmograph. Tested person sits in a cabin with rigid but glassy walls. There are two main types: plethysmograph with constant pressure or with constant volume. Constant pressure is ensured by a piston moving in a tube connected to the cabin. The movement of the piston changes the volume of the system. Whole body plethysmograph makes possible the monitoring of alveolar pressure and so the assessment of breathing resistance. When the shutter in the flow sensor is closed then the volume of the lungs, when it is open then alveolar pressure can be determined. Breathing resistance can be calculated if also air flow is measured.

Figure 9.20. Whole body plethysmograph
http://commons.wikimedia.org/wiki/File:Normal_values_for_FVC,_FEV1_and_FEF_25-75.png author: Mabel J)



5. Problems

1. The tested person performs maximal expiration (the volume of the lungs decreases to RV). The nitrogen concentration in the lungs is 78%. Following maximal expiration the person inhales 100% oxygen until the nitrogen concentration in the lungs drops to 1%. The total air exhaled during the test is 35 l; its nitrogen concentration is 2.2%. Calculate the reserve volume (RV) of the person.
2. Determine the uncertainty of calculation related to problem 1 if the uncertainty of nitrogen concentration measurement is 3%.
3. Evaluate the error that would be caused by omitting BTPS calculation. Calculate with the following parameters: body temperature 37 °C, room temperature 25 °C. During inspiration the pressure in the lungs is by 3 mmHg less; during expiration is 3 mmHg more than room pressure.
4. What parameters are measured by a whole body plethysmograph? What assures constant pressure in the cabin when the person sitting in it breathes?
5. Why do predicted values apply for forced breathing and not for normal breathing?

6. Bibliography

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Chapter 10. Movement analysis

Neurologists observed and described specific changes in the motor coordination of their patients – compared to healthy control subjects – a long time ago. In the early, preclinical phase the subtle changes rarely can be detected by visual inspection. Likewise, small variations in the performance of a patient resulting from the slow progress of the disease remain undetected for the human observer. Evaluation of movement helps the diagnosis – even early diagnosis – and assessment of the actual state of patients if

- the movement patterns and the directions given to tested persons are defined in detail,
- movements are recorded with adequate sampling rate and spatial resolution,
- meaningful parameters are generated by proper feature extraction methods.

Human movement analysis is applied in sports-, rehabilitation- and ergonomic studies.

Visual observation permits only rough (mainly qualitative) evaluation of movements. While human static image processing ability is much-to-be-admired, the details of even simple movements cannot be quantitatively analysed based on visual observation. The task is much simpler if movement can be analysed using still image(s). Figure 10.1 shows an example. Still images were taken from a pole vaulter in every 100 ms using the so called chronophotographic method.

Since Aristotle many researchers have been dealing with movement analysis, even with picturing movements in still images [10.1]. Results of E.-J. Marey (1830 – 1904, French physiologist and scientist) are valuable even today. He is considered to be the father of biomechanics. He recorded movements on cinefilm years before the Lumière brothers. His inventions were meant to serve scientific intentions. He thought it was no use of replaying movements in order to see it again. As a result he is remembered only by those dealing with movement analysis. In 1995 the 100th anniversary of the cinema – and not the cinefilm – was celebrated.

Figure 10.1. Movement of a pole vaulter is pictured in still image (Marey, 1886)
http://stephan.barron.free.fr/art_video/chronophotographie.html

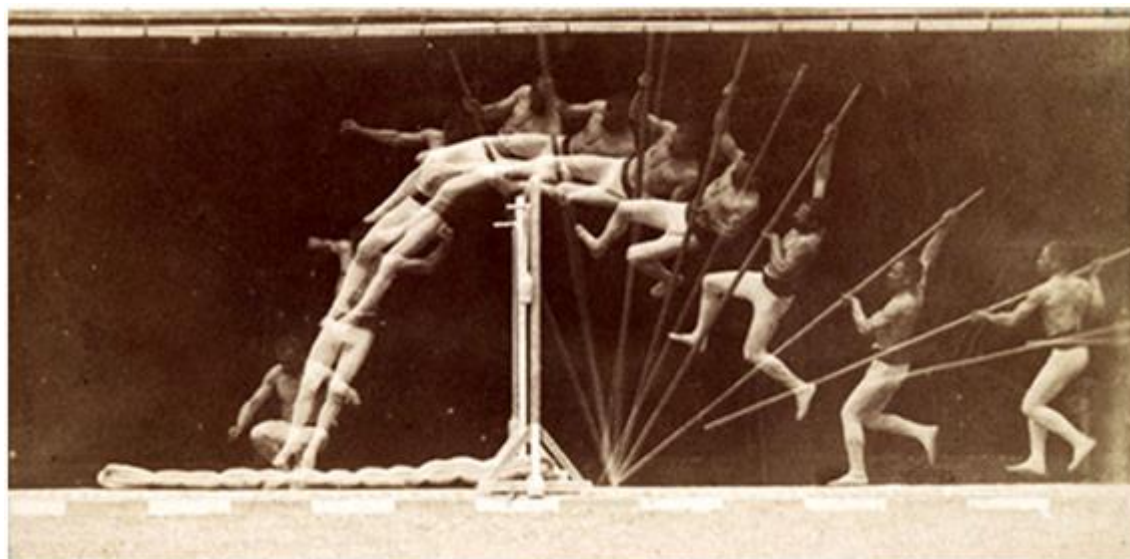


Figure 10.1 demonstrates how movement can be pictured in still image. This solution is simple and cheap but only coarse resolution is achievable. In fact, it only allows for a qualitative assessment. In general, accurate analysis requires three dimensional recording to be taken with several (at least two) cameras. The sampling frequency must also be increased.

Both anatomical and laboratory coordinate system can be used to describe human movements. Anatomical coordinate system is fixed to specified bones; using it we can easily characterise the movement of body segments relative to each other. The CAMARC project (Computer Aided Movement Analysis in a

Rehabilitation Context) [10.7] gave a suggestion for a standard coordinate system fixed to specified bones. It has not been widely accepted yet. Movement of the whole body as well as body segments can be described in the laboratory coordinate system. The prevalent biomechanical models build up the human body from rigid segments [10.4].

1. Devices for human movement analysis

Human movement analysis requires the measurement of the following parameters: displacement, rotation, force, torque. The electrical activity of motor controlling muscles can be measured by an electromyograph (EMG). Goniometer can be applied to measure the angle between two body segments. A simple goniometer is shown in Figure 10.2. Placing a potentiometer into the pivotal point the angle can be transformed into electrical signal and thus continuously monitored. Figure 10.3 shows a single degree of freedom goniometer based on light passing through a pair of optic fibres.

Figure 10.2. Simple goniometer
(http://commons.wikimedia.org/wiki/File:Medizinischer_Goniometer.jpg#file author: Voxymoron)

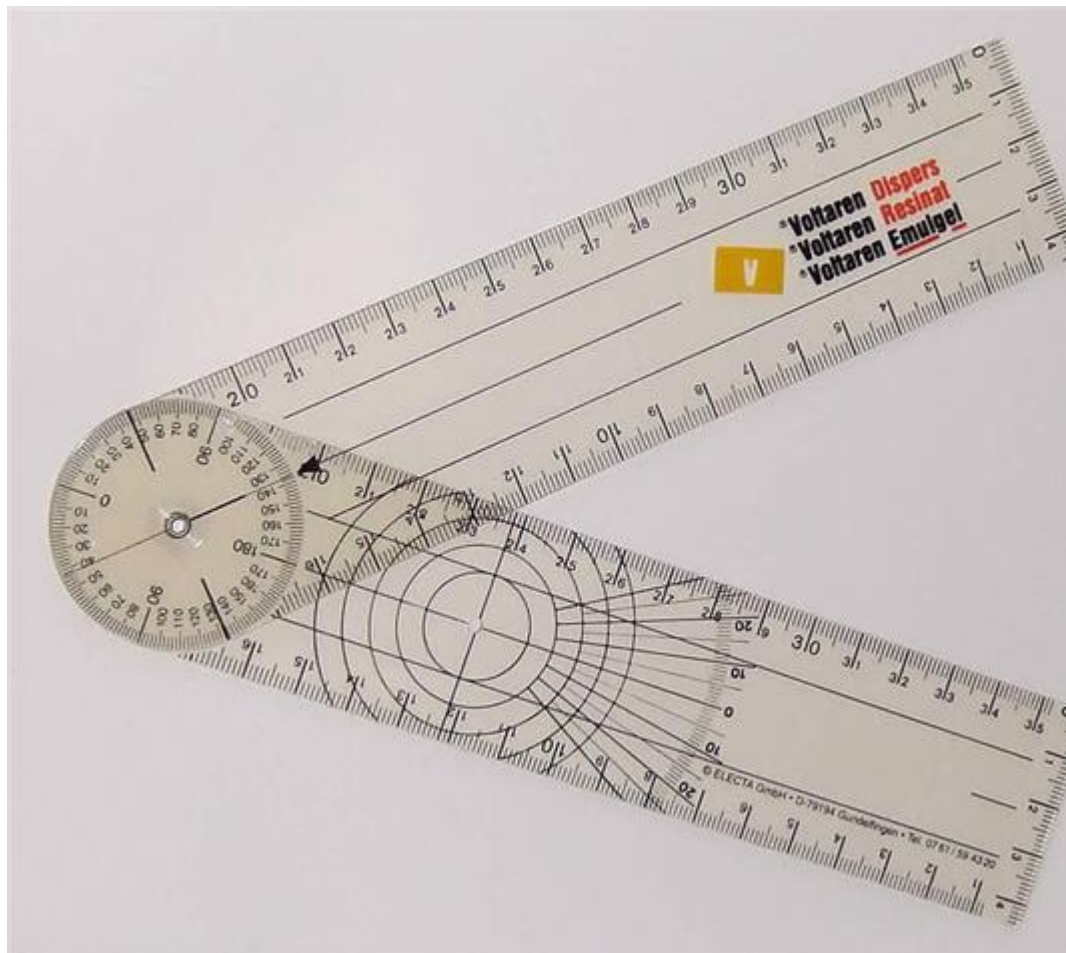


Figure 10.3. Goniometer to measure knee angle of
(<http://www.adinstruments.com/products/mlts700#overview> ADInstruments) (Product of



The kinematic parameters of movements can be assessed by force and/or acceleration measurement. In clinical practice the most widespread devices are: force plate, pedograph, and accelerometer attached to the body or limbs.

The force plate (see Figure 10.4) measures the x, y and z component of the force exerted on it. The pedograph (see Figure 10.5) measures the force distribution of the foot sole. Most frequently it is composed of capacitive sensors. Its planar resolution can be as low as 0.25 mm², the maximum measurable pressure is about 200 N/cm².

Figure 10.4. Force plate [10.2]<http://www.kistler.com/us/en/product/force/9285BA> (Product of Kistler)

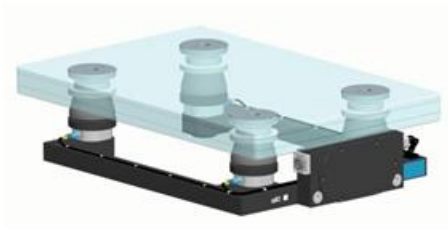
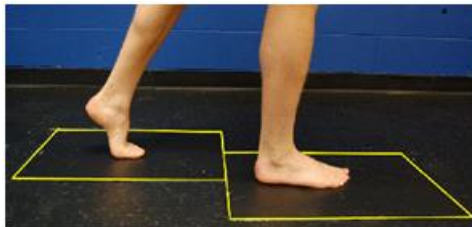


Figure 10.5. Foot sole pressure sensor (pedograph) <http://podiatry.temple.edu/gaitlab/facilities/kistler.html> (Product of Kistler)



Based on the signals of a three dimensional accelerometer (see Figure 10.6) its displacement from a starting position cannot be determined unambiguously. In the general case infinite number of different six degrees of freedom movements can result in the accelerations measured in three directions (x, y and z). This is also an inverse problem (see chapter 6.7). Having enough a priori information can help to characterise a six degrees of freedom movement based on the output signal of a single three dimensional accelerometer. Attaching more accelerometers to a limb can promote the solving of the inverse problem. Sensors integrating accelerometer, magnetometer and gyroscope (sensor fusion) give much better estimate on position and actual angle.

Figure 10.6. Three dimensional accelerometer module (DE ACCM3D, 21 x 10 mm) <http://www.dimensionengineering.com/products/de-accm3d> (Product of Dimension Engineering)

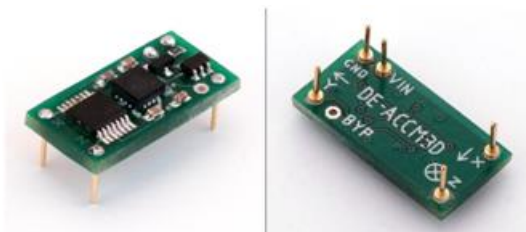
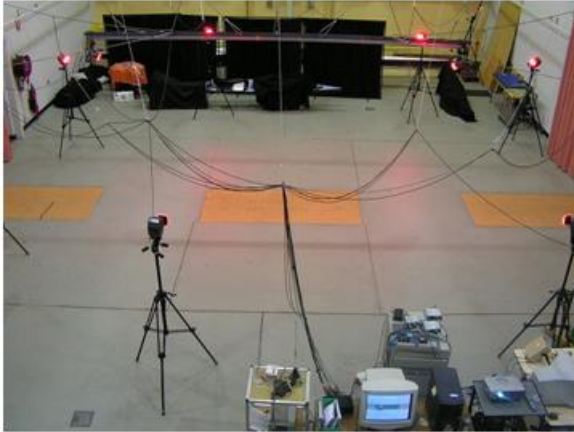


Figure 10.7 shows a modern gait analysis lab. Contact pressures and forces under the sole of the foot are measured by force plates, movement of body segments can be determined by tracking passive markers attached to anatomical landmark points. Markers are tracked by ten cameras so the masking effect (markers by limbs) is minimal.

Figure 10.7. Gait analysis lab with force plates and infrared cameras
http://en.wikipedia.org/wiki/File:Gait_laboratory.jpg (author: Robertson DGE)



In this chapter only passive marker based movement analysis is dealt with. It must be noted that marker free movement analysis can also be applied both with video based analysers and with mechanical or magnetic position sensors.

2. Marker based movement analysis

Figure 10.8. Passive markers to be attached to the wrist (above) and finger (below) with elastic band



Passive markers are shown in Figure 10.8. These markers reflect the incident light. They are covered with retroreflective material thus reflect the light to the same direction where it came from. This is assured by the refraction coefficient of the micro spheres in the material (see Figure 10.9).

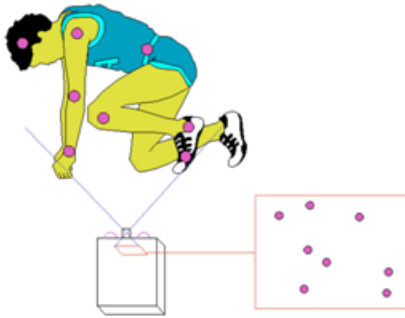
Figure 10.9. The micro spheres in the retroreflective material (with appropriate refraction coefficient) reflect the light to the same direction where it came from



Passive markers are lightweight, do not need power and cause no discomfort to the tested person. As a result they negligibly affect the tested movement. When a frame is recorded then all marker images are taken at the same time. Their disadvantage is that each marker has to be identified on each frame taken.

Active markers have their own light. These are easily identified as only one marker is lit at a time. The disadvantage of active markers is that they must be powered: either through wiring or with a local energy source. When several markers are attached to a moving person then the time delays between flashing them means that the positions of markers are not known at the same time. This has to be taken into account during data processing.

Figure 10.10. The marker pattern (right below) is the information characterising a given movement phase (left above)



Markers are attached to anatomical landmark points. The movement analyser will determine the marker positions (see Figure 10.10) with the sampling frequency. Movement is characterised based on the marker trajectories. Determining the marker positions i.e. anatomical landmark points is decisive for the efficient analysis. A widely accepted (standard) marker pattern would increase the comparability of the results and so the medical application of movement analysis.

Figure 10.11. Marker pattern for gait analysis

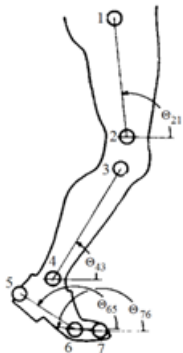


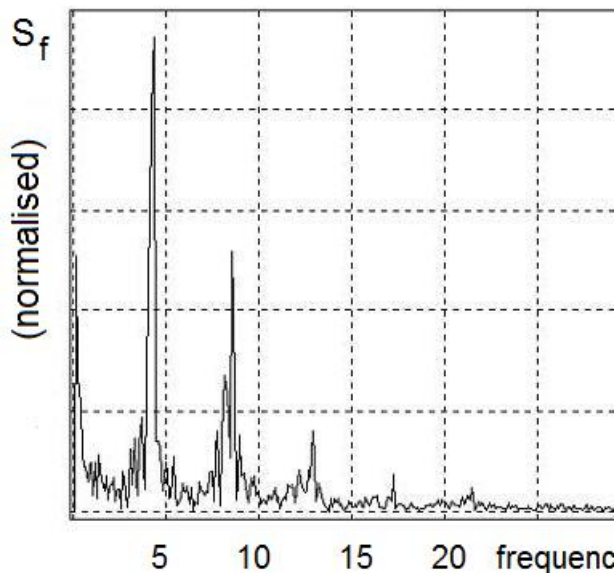
Figure 10.11 shows a possible marker pattern on one leg for gait analysis. The figure also shows the usual definitions for angles. $\Theta_{\text{thigh}} = \Theta_{21}$, $\Theta_{\text{knee}} = \Theta_{21} - \Theta_{43}$, $\Theta_{\text{shank}} = \Theta_{43}$, $\Theta_{\text{ankle}} = \Theta_{43} - \Theta_{65} + 90^\circ$. There is no single standard marker pattern for gait analysis. Different laboratories use 14, 15, 19 or 23 anatomical landmark points placed from toe to hip [10.3], [10.4].

2.1. The necessary sampling frequency

Image based movement analysers sample the marker positions. Thus theorems of sampling must be taken into account. However, low-pass filtering in the optical domain preceding sampling is not possible. The minimal necessary sampling rate must be determined before movement analysis by examining the movement pattern. 24 samples/second is considered to be enough for the analysis of normal and pathologic gait by [10.15]. This is the sampling frequency of cine cameras. Widely used video cameras use 25 full and 50 half frames per second. There are electromagnetic (e.g. Flock of Birds by Polhemus) and ultrasound based (e.g. Zebris) movement analysers [10.16]. The finger tapping movement was recorded with a 100 frames/s Precision Motion Analysis System, PRIMAS [10.5]. The trajectory of the marker on the little finger of a young healthy male is given in Figure 10.12. Based on a number of similar recordings 50 frames/s is enough for studying the finger tapping movement. The necessary sampling rate was analysed also by evaluating the finger tapping movement. Data recorded with 100 samples/s sampling rate was processed and the parameters characterizing the movement were determined using the complete database as well as reduced databases. The database was reduced in two steps.

First every second data was eliminated. The resulting database has a 50 frames/s sampling rate. In the second step every second data was eliminated again. This results in a 25 frames/s frame rate. Thus there are three databases with three different sampling rates taken from the same movement. The algorithms evaluating finger tapping (see section 10.3.1) calculated practically similar values using the 100 samples/ and the 50 samples/s databases. The values calculated from the 25 samples/s database were significantly different. This confirms that 50 samples/s sampling rate is enough for testing finger-, hand- arm- and leg movements for medical purposes.

Figure 10.12. Frequency spectrum of the marker attached to little finger during finger tapping



2.2. Marker attachment, marker image processing

For human movement analysis marker attachment is difficult. Double sided adhesive tape is inappropriate for this purpose. The reason is that skin can easily move from the anatomical landmark point. At the wrist skin movement can be 2 cm! Most frequently elastic band is used to attach markers. Figure 10.13 shows markers attached to the second phalanxes for finger tapping test.

Figure 10.13. Markers attached to fingers with elastic band

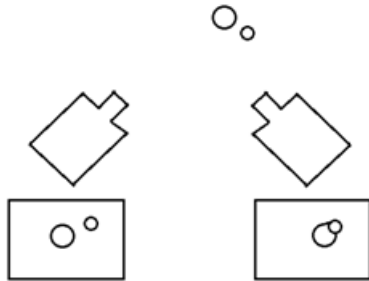


Researchers studied the possibility to fix markers to bones with pins applying local anaesthesia. The research to develop limb prosthesis was carried out at College of Engineering, University of California, Berkeley between 1945 and 1947. The evaluation of the research [10.17] clearly shows that this way of marker attachment cannot be used in routine clinical practice.

The marker has a finite volume. Image based movement analysers determine the actual position of a certain parameter of the marker. During the movement the camera looks at the marker from various directions. It follows that the optimal marker shape is the sphere and parameter to be determined is its centre point. (For two dimensional studies, e.g. face tremor assessment disk shaped markers can be used.) The three dimensional marker has a two dimensional projection on the camera sensor. The centre point of the marker image must be determined based on the intensities of pixels fully or partly covered by the marker image. For a single camera the line is determined that connects the marker and the marker image centre point. A marker anywhere along

this line results in the same centre point on the sensor. The animation illustrating this can be found at: http://project.mit.bme.hu/kobak2012/marker_markerimage.pps. To determine the spatial position of a marker at least two cameras are needed, see Figure 10.14.

Figure 10.14. Two markers and their projections on the sensors of two cameras



Nearly all presently used image based movement analysers have CCD sensors. To determine their resolution it is not enough to know the number of pixels in the sensors. When a marker image covers fully or partly several pixels then the centre of the marker image can be determined with subpixel resolution. Resulting from the quantisation the centre of the marker image can only be estimated. The estimation methods are detailed in [10.18].

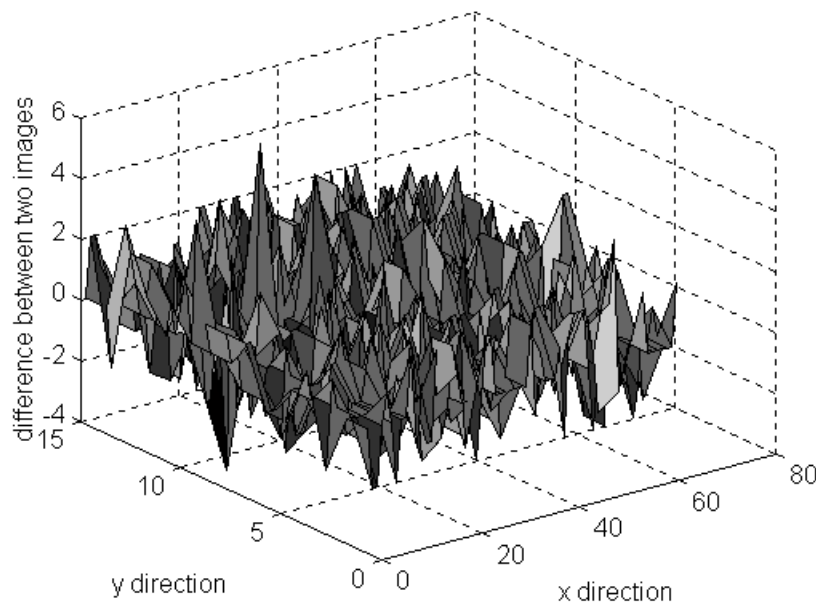
2.3. Resolution, accuracy and precision (reproducibility)

These parameters are defined according to [10.19]. Resolution of a motion analyser is the smallest detectable displacement or the longest undetectable displacement. Accuracy is the degree of agreement between individual measurements and accepted reference values. Accuracy is a measure of systematic error. Precision is the degree of mutual agreement among repeated observations made under identical conditions (both camera and marker in constant position). Precision is a measure of random error. Precision characterises the stability (repro-ducibility) of the system. High precision is necessary, but not satisfactory condition for high accuracy.

These parameters cannot be given as single constants for an image-based analyser, because they strongly depend on the marker image size. If the marker image covers more pixels, accuracy, precision and resolution are more favourable. The nonlinearity of the lens also influences these parameters; worst results can be expected when marker images appear in the corners of the FOV.

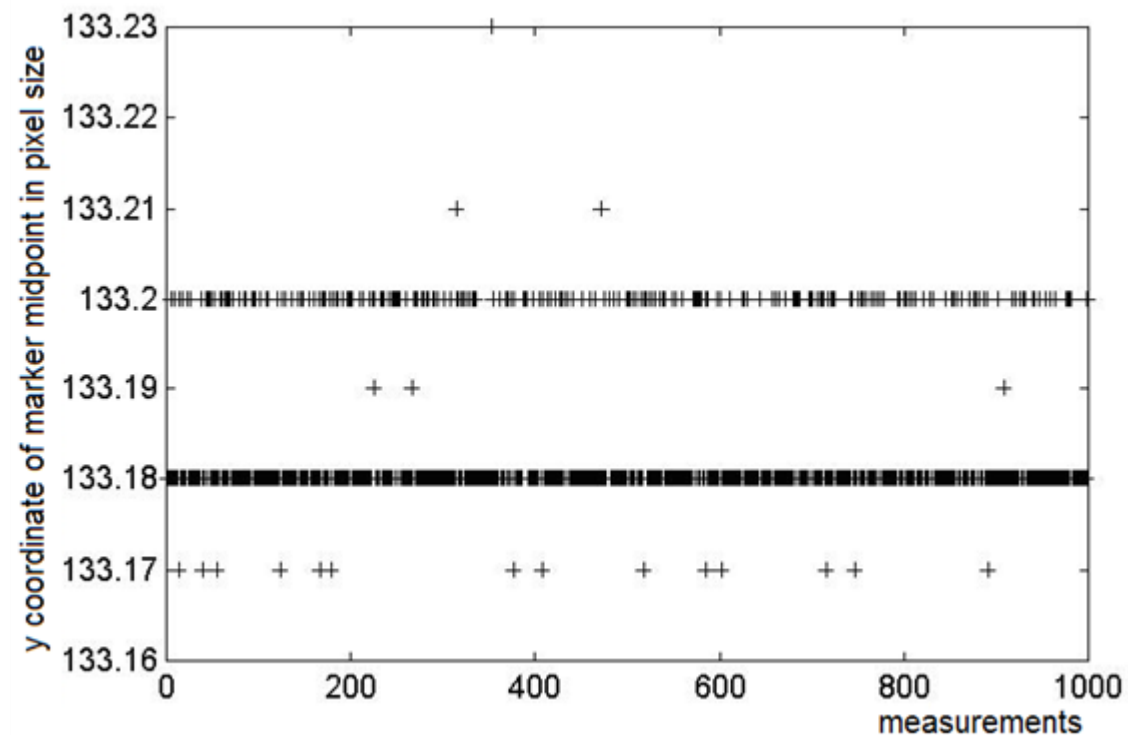
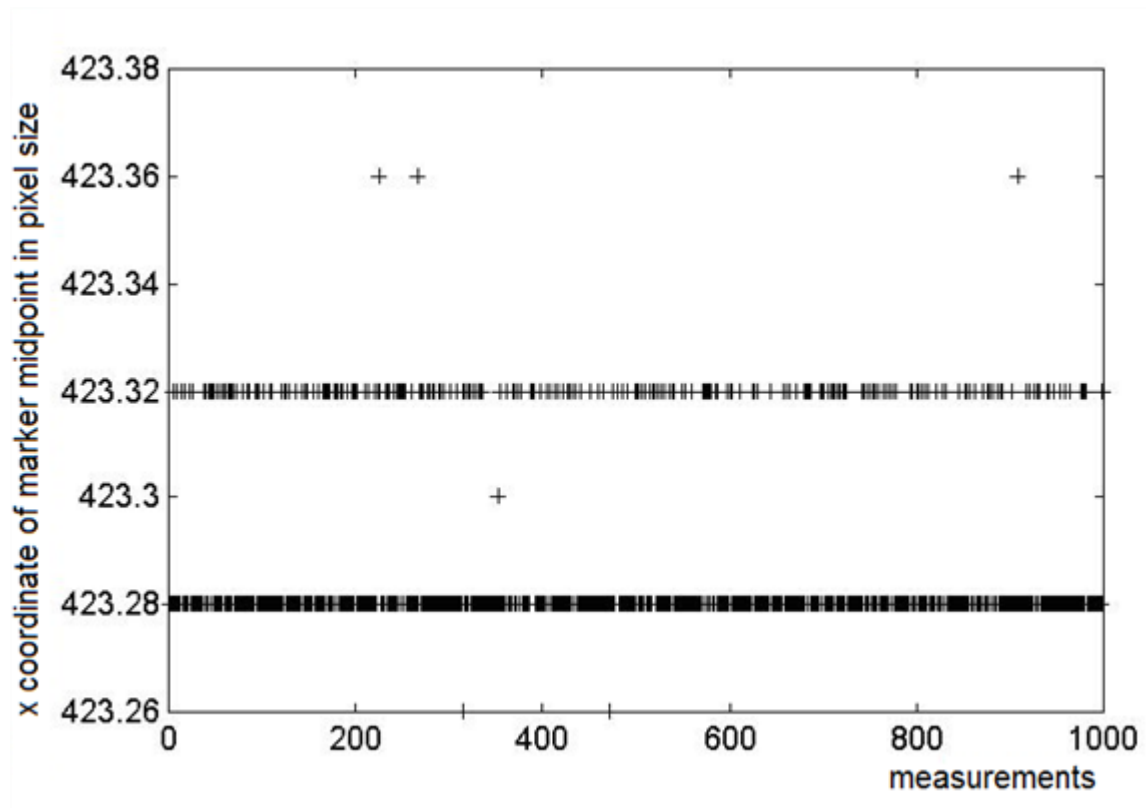
Each application requires a dedicated preliminary evaluation to check if the analyser is able to meet the requirements. The analysis of human movements in the medical care rarely demands high accuracy or precision.

Figure 10.15. Noise of a CCD sensor: the difference of two images taken from the same scene. Tested sensor is Philips BXA 1011; images were digitised using 8-bit A/D converter



The noise of the sensor influences all the three parameters. The camera of the PRIMAS motion analyser was tested. Its frame transfer sensor is Philips NXA 1011 with 604 x 288 pixels able to operate with 100 frames per second. The evaluation of the marker image is supported by hardware. Binary marker image is generated by thresholding the video signal. The video/(digital coordinate) converter detects the pixels covered by the marker image. This conversion method had been first applied by E.H. Furnée [10.20]; later it was incorporated into several analysers. A 64 x 16 pixels part of the PRIMAS HTH MX camera sensor was tested with an 8-bit flash A/D converter. Differential images were produced when the camera and the marker were in fixed position. Figure 10.15 shows a typical differential image. While taking the two images there were two markers in the FOV of the camera. These cannot be identified in the differential image. Various static images were analysed including complete darkness. The maximum pixel intensity was 255, the differential images had values between -5 and +5 independent of the actual static image.

Figure 10.16. Variation of the measured centre point of a static marker image during a 10-s recording

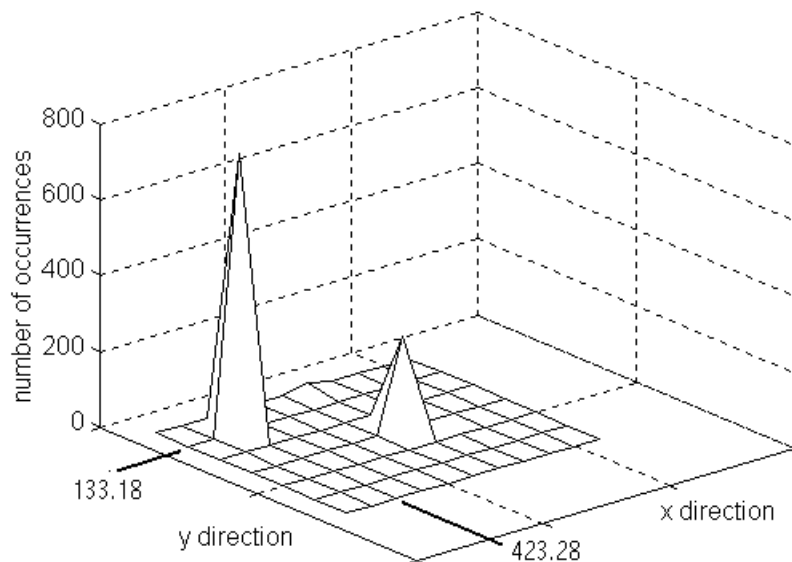


Measurement of the resolution requires well defined reproducible small displacement of a marker. This can be produced with a marker attached to a micrometer (micrometer screw gauge) or to the printing head of a matrix printer. The printing head of the TECO VP2450 can be set into 775 different positions; there is a constant distance (0.419 mm) between two adjacent positions. The maximum displacement of the printing head is 325 mm. A ping-pong ball size marker was attached to the printing head which was (in its middle position) 375 cm far from the sensor of the camera. In the vertical plane of the movement of the printing head the FOV of the camera was 365 x 271 cm. As a result the minimal displacement of the marker was 1/8711 compared to the

horizontal side of the FOV. The marker – being so far from the camera – resulted in an unusually small marker image covering 8 – 10 pixels. The printing head was moved to 10 adjacent positions from left to right and then back. On the way there and back the marker being in the same position resulted in centre values with good agreement. This means the printing head could be set to different positions with high precision. The standard deviation of the centre values in a given position was much smaller than the difference of marker centres in adjacent positions. It follows that the marker in two adjacent positions resulted in clearly distinct centre values. Thus the horizontal resolution is better than 1/8711. Refinement of resolution assessment requires smaller reproducible displacement or increased camera – marker distance.

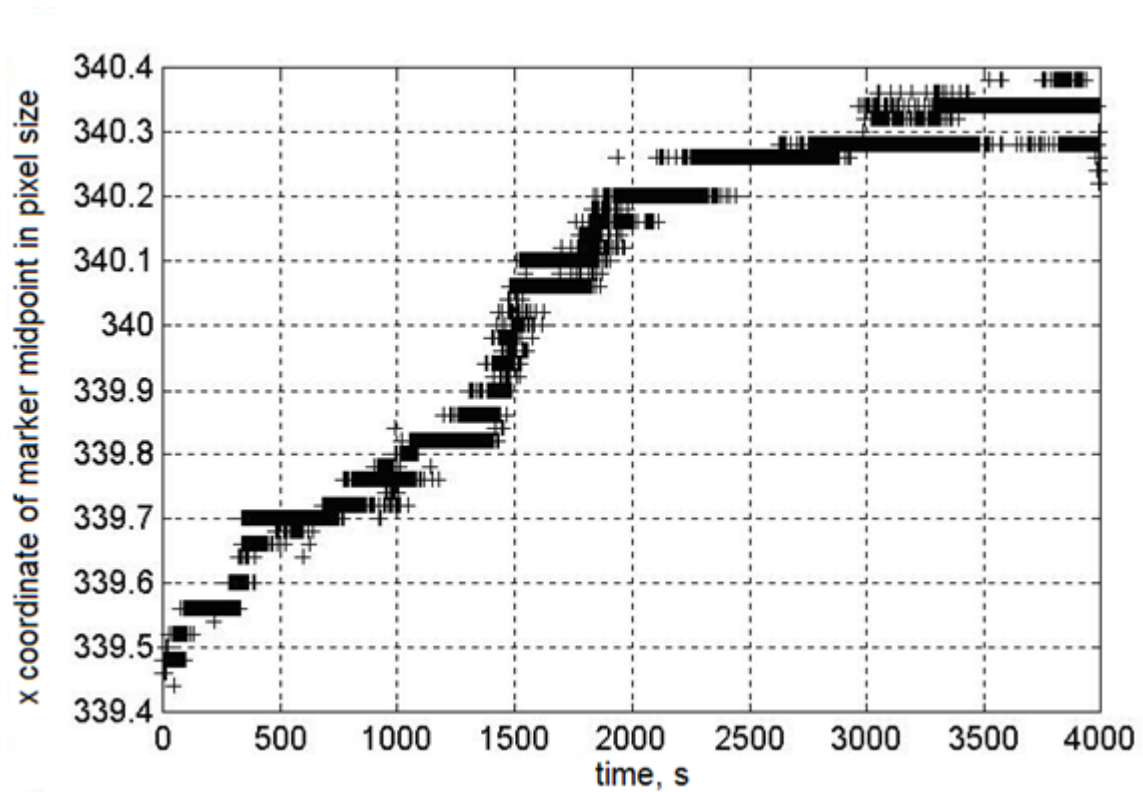
Precision (reproducibility) is influenced mainly by noise. However, warming up of the camera cannot be neglected. To characterise short-term stability of marker centre estimation 10-s recordings were taken from static markers. PRIMAS movement analyser was used with 100 frames/s sampling rate. This means 1000 marker centre positions. The estimated horizontal and vertical centre coordinates over time are shown in Figure 10.16. Based on it, the estimated centre over plane is shown in Figure 10.17. It is clearly not a normal distribution. For 99.7 % of estimated centre values the maximum horizontal deviation is 0.04 pixel side. The sensor has 604 columns so 0.04 pixel side means a horizontal precision of 1/15100 (compared to the horizontal pixel side). For 99.8 % of estimated centre values the maximum vertical deviation is 0.03 pixel side. The sensor has 288 rows so 0.03 pixel side means a vertical precision of 1/9600.

Figure 10.17. Deviation of the estimated centre of a static marker



Following turning on, the warming up of the camera shifts the estimated horizontal coordinate of a static marker by a pixel side. This means 1/600 to FOV, an order of magnitude worse than short time reproducibility (precision)!

Figure 10.18. Changing of the estimated horizontal coordinate of static marker midpoint during the first hour after turning on the camera



Accuracy can be tested with markers in known positions of the coordinate system attached to the camera. Instead, accuracy of marker based motion analysers are tested with markers being at a known distance from each other (e.g. fixed to the two ends of a rod) or by moving a marker along a known path. Accuracy of three dimensional analysers can be tested using both methods. Accuracy of two dimensional analysers is rather tested by a marker moving along a known path. This makes possible the assessment of accuracy without exactly knowing marker positions. The set-up described in testing resolution is applicable also for testing accuracy. The measured marker image centre positions are given in Figure 10.19, the deviations from a straight line are shown in Figure 10.20. Mainly because of lens distortion, the deviation strongly depends on the position of the marker image on the sensor.

Image based motion analysers separate marker images from the background based on their brightness. Passive marker based analysers flash IR LEDs around the camera in pulsed mode. Flashing the LEDs is synchronised to the integration of the CCD sensor. This increases ambient light suppression. 100 frames/s means 10 ms for making one frame. If IR LEDs are lit for 250 μ s and the CCD sensor integrates the light on its pixels for the same time then the light reflected from the markers is present during the total integration time. When IR LEDs are off then integration is also off. Ambient light is integrated only in 1/40 part of the total frame time. When an object (e.g. ring, wrist watch) reflects the IR light beam it can be erroneously identified as a marker. The definition of the spatial position of a marker requires at least two cameras.

Figure 10.19. Centre positions of a marker (+) moving along a straight line

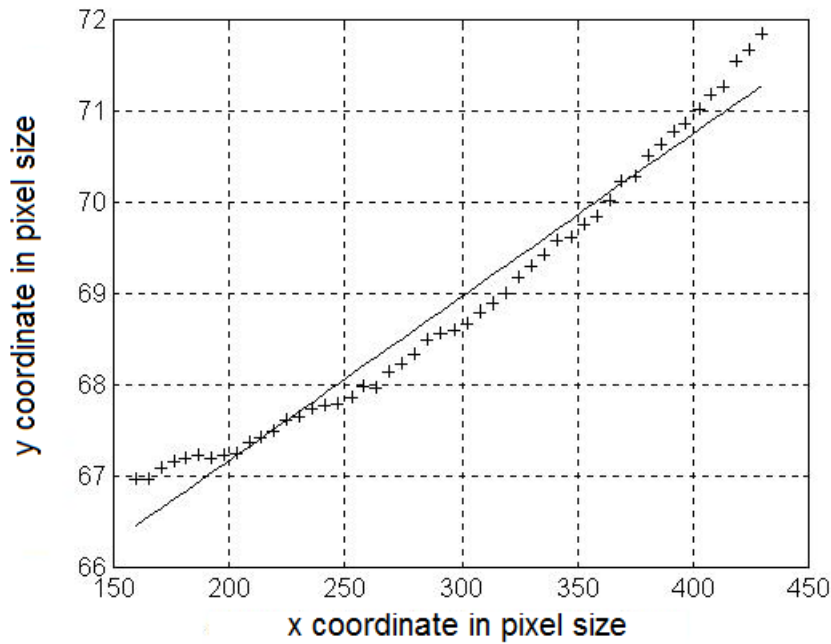
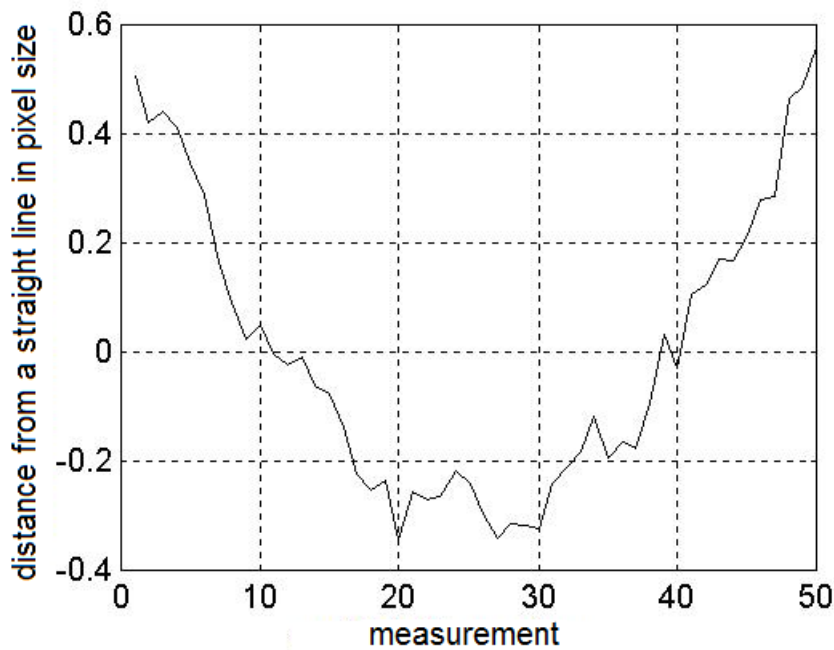


Figure 10.20. Deviation of the centre positions of the marker from the straight line



User programs process marker centre coordinates to determine parameters important in a given application. Centre points of digital marker images can be estimated using different algorithms. The most common method is the calculation of geometric centroid, see eq. 10.1.

$$X_{0g} = \frac{1}{N} \sum_{j=1}^N x_j, \quad Y_{0g} = \frac{1}{N} \sum_{j=1}^N y_j \quad (10.1)$$

where x_j , y_j is the centre point of the j th pixel of the binary image covered by the marker image; X_{0g} , Y_{0g} is the estimated centre point. The method can be extended to graded images. Pixel midpoints should be weighted by the intensity of the pixel.

The marker is projected to different positions on the sensor of a camera depending on the camera – marker relative position. If the marker is in the FOV of at least two cameras and the positions of the cameras to each other are known then the spatial (three dimensional) coordinates of the marker can be determined. The positions of the cameras to each other must be determined accurately during calibration. Markers attached to a rigid construction should cover the whole space of the movement. Often the calibration object is dismountable; built up using sticks and rods.

There are image (video) based motion analysers exceeding 1000 frame/s frame rate. The VICON T10S camera has a 1 Mpixel sensor. The maximum frame rate with full resolution is 1000 frames/s, with partial resolution (only a part of the sensor is used) 2000 frames/s.

Figure 10.21. Passive marker based motion analyser (PAM) for clinical application



Figure 10.22. The camera of PAM with IR optical filter and IR LED ring



Figure 10.21 shows a passive marker based movement analyser (PAM) applicable for clinical use [10.6]. Figure 10.22 shows the IR LED ring and the optical filter (B+W O93) of the PAM camera. The optical filter passes the 885 nm IR light and attenuates visible light. PAM has a single camera thus it is able to assess movements if the marker trajectories are limited to a narrow volume. Clinical application is aided by the simple operator interface, small size and its low price. Video recordings of finger tapping (both stroke patients and healthy control subjects), facial tremor and limb tremor belonging to the ON and OFF state of a brain pacemaker are available:

http://project.mit.bme.hu/kobak2012/Fingertapping_stroke.wmv

http://project.mit.bme.hu/kobak2012/Fingertapping_healthy.wmv

http://project.mit.bme.hu/kobak2012/Facial_tremor.wmv

http://project.mit.bme.hu/kobak2012/Brain_pacemaker.wmv

3. Movement analysis in medical practice

3.1. Finger tapping movement

Related to this movement it is described how to develop a procedure for the objective assessment of the actual state of patients. In clinical movement analysis the following are important in general: the movement pattern must be defined in detail (including the instruction given to the tested person); a method for the evaluation of quasiperiodic marker trajectories; tested persons need some time to learn the movement before testing; both the definition and the evaluation of the movement pattern can be personalised. This movement was studied already in the 19th century to assess motor coordination [10.9]. In the clinical practice this movement is observed visually. Only experienced observers can qualify the movement, even they are unable to pinpoint subtle changes. There are simple contact sensors [10.10] which detect touch of the tabletop. By these sensors the time between two touches and the number of touches within a given time can be measured (see Figure 10.23).

Figure 10.23. Recording finger tapping movement using passive markers and contact sensors



Finger tapping can be performed with a single finger. In clinical practice the most often used version of the test is executed with eight fingers. In the starting position both hands (wrists and fingers) are on the tabletop. Fingers (except thumbs) are lifted at the same time at least by a 30 degree angle so that wrists remain on the tabletop. Then the fingers hit the table in the following order: little finger – ring finger – middle finger – index finger. (The order might be the other way round from index finger to little finger.) When all fingers hit the table at the same time the test is called hand tapping. When markers are attached to the fingers then their movement can be monitored during the whole test, not only the moment of hitting the tabletop is known (see Figure 10.24).

Figure 10.24. The finger tapping movement. Markers attached to the fingers can be tracked during the complete movement



Based on the marker trajectories the movement can be analysed in detail. Greater amplitude and/or faster movement means better performance. It is obvious – readers are suggested trying it out – that the movement can be executed faster with smaller amplitude. The speed of the movement is best characterised by the product of amplitude and frequency, the parameter is called *amxfr*. Its average over the complete test is given by eq. 10.2.

$$amxfr = \frac{\sum_{i=1}^n \frac{A_i}{T_i}}{n} \quad (10.2)$$

where A_i is the amplitude of the i th cycle in cm; T_i is the length of the i th cycle (time between two table contacts) in s; n is the number of cycles during the test; *amxfr* is the calculated parameter characterising the speed of the movement in cm/s. The similarity of the cycles is also an important parameter of motor coordination. Similarity is well characterised by PM (periodicity of movement, see section 4.2.5). It is also evident (this is also suggested trying out) that it is easier to produce similar cycles if the movement is slower. Taking all these into account the movement of a finger is well characterised by the FTTS (finger tapping test score) parameter which is the product of speed and regularity. Based on the evaluation of more than 300 recordings taken from Parkinsonians and healthy control subjects [10.11] the relative weight of PM is suggested being shifted by 0.6 (see eq. 10.3).

$$FTTS = (PM - 0.6) \cdot amxfr \quad (10.3)$$

PM was greater than 0.6 for all healthy control subjects and for the majority of Parkinsonians. PM is dimensionless, thus FTTS is in cm/s. Based on the FTTS values of all fingers the FTTS of a hand and of the tested person (for both hands) can be calculated. The neurologist supervising the movement analysis can personalise the evaluation of the finger tapping test. It may happen that the neurologist wants to know the performance of a few fingers only. Most often the movement of the little finger has no diagnostic value, its movement is neglected. Figures 10.22 – 10.25 illustrate the finger tapping movement of four different persons. The upper two subfigures show the trajectories of right and left ring (solid line), middle (dashed line) and index (dotted line) fingers during 1.5 s. The lower two subfigures show the trajectories of the right and left middle fingers for 8 s. Even the young healthy subject does not produce periodic signals (see Figure 10.25) but the trajectories of fingers of the two hands are very similar. Parkinsonian patients both P07 (see Figure 10.26) and P08 (Figure 10.27) were in the early stage of the disease (0-1 stage according to the modified Hoehn-Yahr scale). However, they performed the test completely differently. This confirms the observation of neurologists that each Parkinsonian exhibits unique symptoms. P07 hardly falls short to the average of healthy subjects. Her right side is affected. With her right fingers she produced smaller amplitudes and in the second cycle in Figure 10.26 she produced a small jerk especially with her ring finger. The time intervals between table contacts vary for her right fingers.

Figure 10.25. Finger tapping movement of a young healthy subject

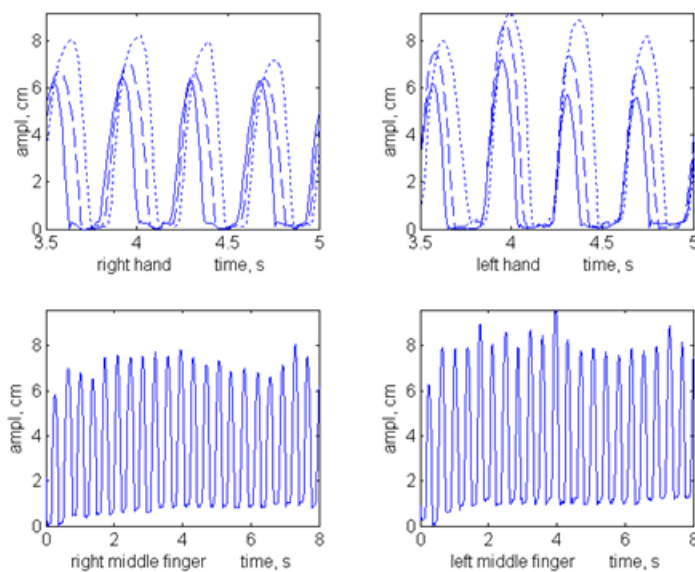


Figure 10.26. Finger tapping movement of a Parkinsonian patient being in the early stage (P07, Figure 10.24.)

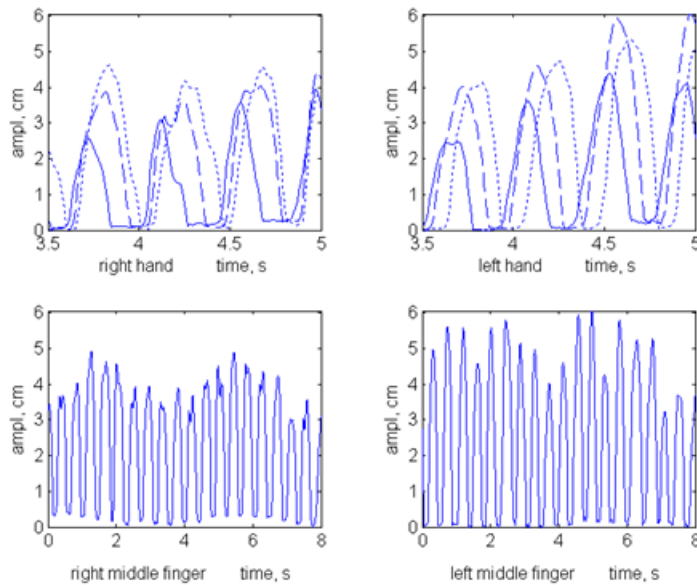
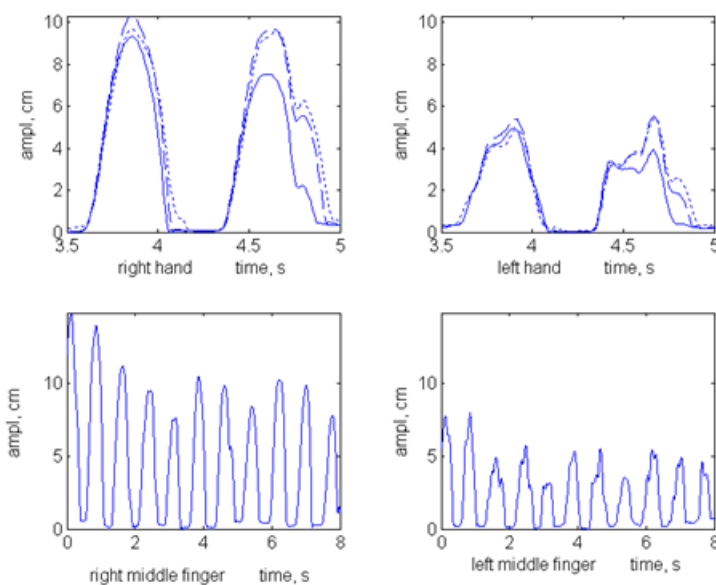


Figure 10.27. Finger tapping movement of a Parkinsonian patient being in the early stage (P08, he was diagnosed to be in the same Hoehn-Yahr stage as patient P07)



The movement of patient P08 was significantly slower than that of P07. During 1.5 s he performed only two cycles. His left side was affected to a greater extent. The amplitudes of his left fingers were around the half of his right fingers. Essentially he performed hand tapping; his fingers were lifted in parallel and hit the table also at the same time.

Figure 10.28 shows the movement of a Parkinsonian (P01) in the 1-2 stage of the Hoehn-Yahr scale. His left side was strongly affected. In his right side the index finger moved in opposite phase to his ring and middle fingers.

Figure 10.28. Finger tapping of a Parkinsonian patient (P01) being in advanced stage (H-Y 1-2)

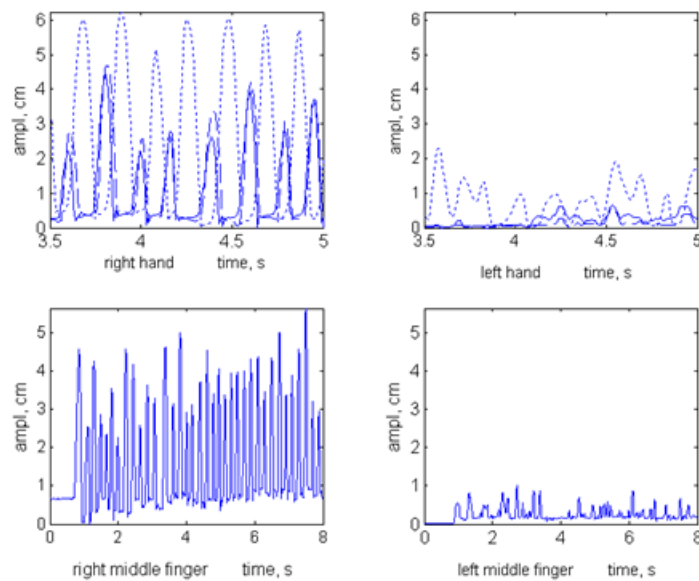


Figure 10.29. FTTS values of Parkinsonian patients averaged for their left (lilac) and right (grey) hands

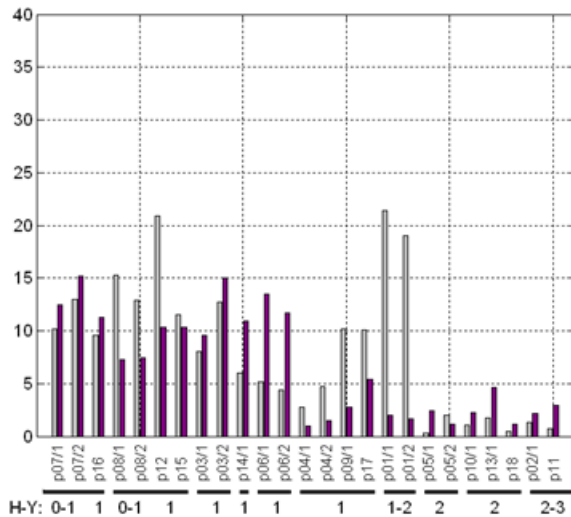


Figure 10.29 shows FTTS values averaged for left and right hands. Patients along the horizontal axis are ordered according to their Hoehn-Yahr stage diagnosed by neurologists. Thick lines span over the results of the same patient. The same patient was given a new identifier when he/she was tested again one or two years later (P07 and P16 is the same person). By the time of a new test one or two years later the Hoehn-Yahr stage of the patient could have changed.

According to the experiences tested persons (both Parkinsonian and stroke patients and healthy subjects) learn the test (how to perform the tapping test efficiently) by the third attempt. Figure 10.30 shows the results of eight tests performed by a young healthy female during a week.

Figure 10.30. Learning can improve the performance. FTTS values of a young healthy female during a week

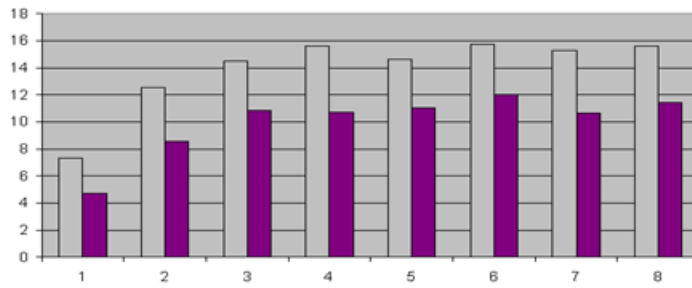
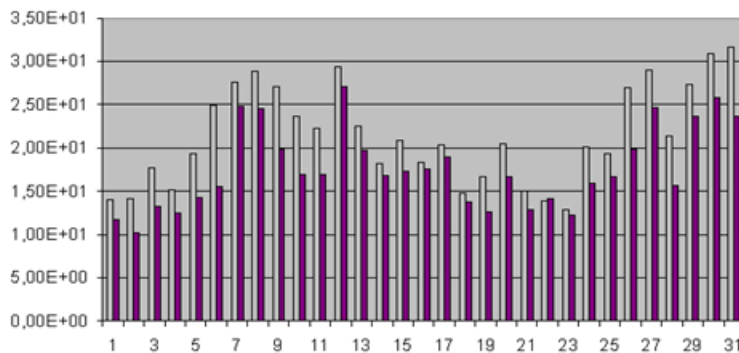


Figure 10.31. The performance (and so the FTTS parameter) can fluctuate. The results of a young healthy male during one month. The results of two tests performed with a 15-minute break may deviate by 25% (17th and 18th tests)



The performance and so the FTTS values can fluctuate even within a short time (see Figure 10.31). The reason can be different; stress level surely influences the result. During clinical movement tests patients' stress level should be low.

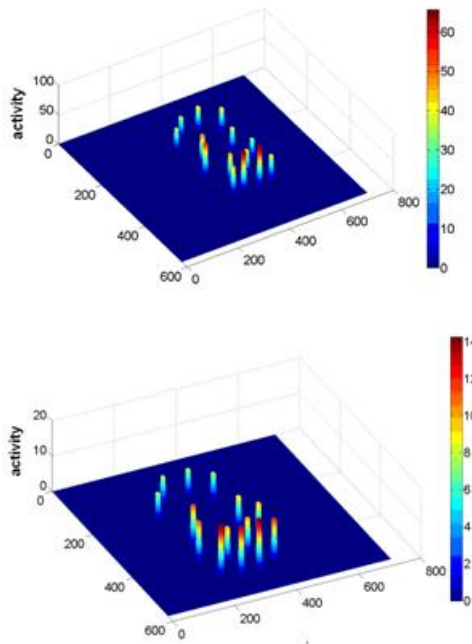
3.2. Facial tremor

Facial tremor can be assessed by attaching disk shaped markers [10.12] to the face. This allows the quantitative characterisation of the actual state of patients with Meige syndrome [10.13]. Measuring the facial tremor with electromyograph is burdensome and the electrodes attached influence the tremor to be measured. Figure 10.32 shows where the neurologist placed 17 markers. Figure 10.33 shows the activity (movement) of markers on the face before and after brain surgery. Surgery attenuated the tremor by an order of magnitude.

Figure 10.32. Marker pattern used to assess facial tremor

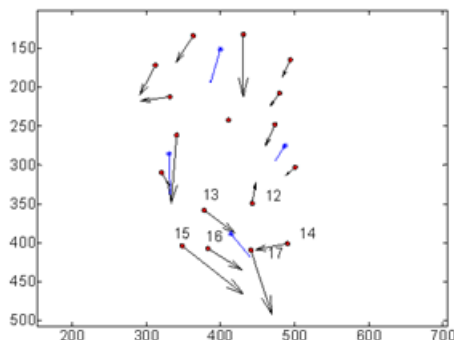


Figure 10.33. Activity of markers shown in Figure 10.32 before (above) and after (below) brain surgery. Scaling of the two subfigures differ by 5:1



Activity of markers in Figure 10.33 is characterised by the total distance covered during the recording with the PAM analyser. Figure 10.34 shows the displacement of markers between two frames (the difference is 20 ms). The tested patient moved her head basically down and to the right. As a result of facial tremor, some markers moved to the opposite direction (e.g. marker no. 12).

Figure 10.34. Displacement of markers on the face during 20 ms



3.3. Hand tremor

Tremor is a rhythmic, involuntary oscillatory muscular contraction, affecting a part of the body [10.14]. Tremor is not a separate disease it is a symptom. It may concern the legs, body, head, limbs, even vocal cords. There are different classification methods for tremor. There are five categories: resting, postural, kinetic or intention (action), task-specific and psychogenic tremor. Even all healthy persons exhibit tremor though it's not always possible to perceive it by visual observation. Attaching markers to the body segment very small amplitude tremor can be revealed. The movement of a marker attached to the index finger of a senior healthy male is shown in Figure 10.35 (outstretched hand); in Figure 10.36 (supported elbow) and in Figure 10.37 (supported wrist). The scaling of the figures is different!

Figure 10.35. Tremor of a senior healthy male, marker on the index finger (outstretched hand). Left: eyes open, right: eyes closed

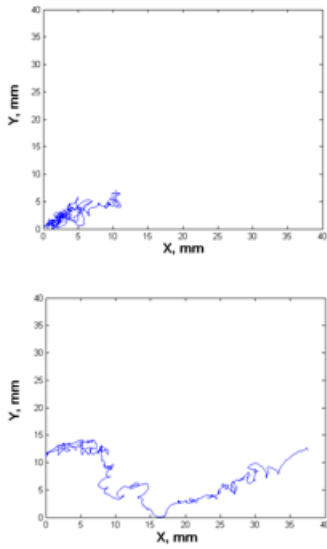


Figure 10.36. Tremor of a senior healthy male, marker on the index finger (supported elbow). Left: eyes open, right: eyes closed

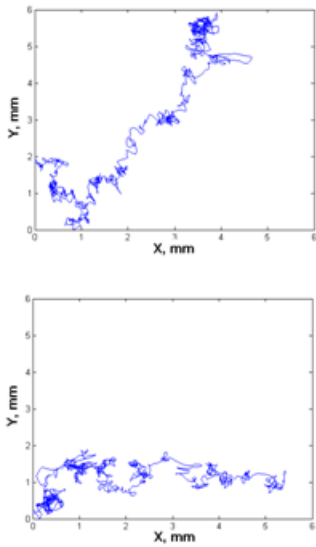
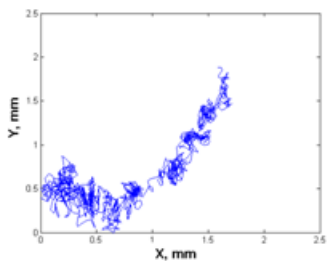
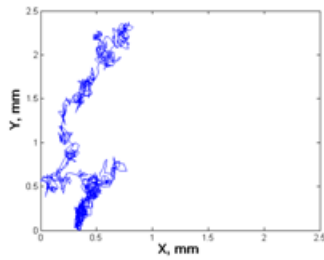


Figure 10.37. Tremor of a senior healthy male, marker on the index finger (supported wrist). Left: eyes open, right: eyes closed





The scaling of the Figures 10.35 – 10.37 is different! Without supporting the elbow or wrist the displacement of the marker is substantially bigger. The smallest marker displacement belongs to supported wrist; but within 20 s even so a 2 mm shift is present.

Figure 10.38. Frequency spectra of trajectories shown in Figure 10.35

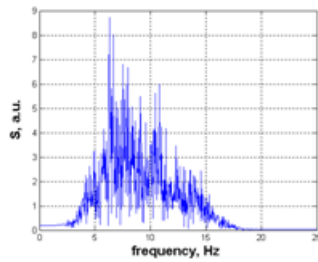
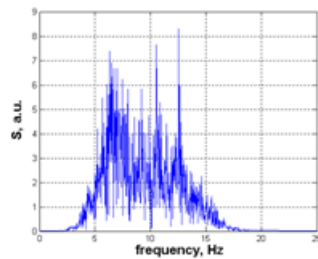


Figure 10.39. Frequency spectra of trajectories shown in Figure 10.36

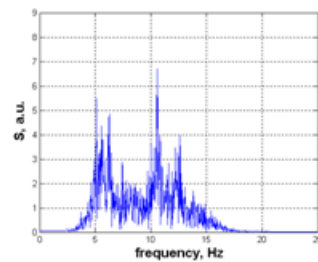
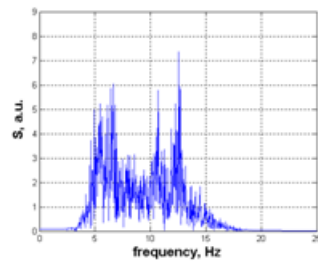
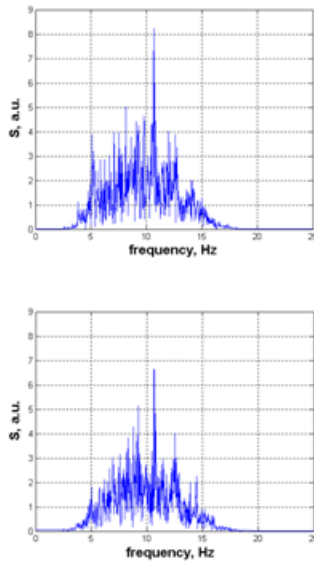


Figure 10.40. Frequency spectra of trajectories shown in Figure 10.37



Figures 10.38 – 10.40 show the frequency spectra of marker trajectories shown in Figures 10.35 – 10.37. With eyes closed the shift of the index finger is substantially greater than with eyes open. This is a low frequency effect.

4. Problems

1. The trajectory of a marker attached to the upper arm of a sportsman needs to be recorded. The maximum velocity of the marker is 10 m/s. The optical axis of the camera is perpendicular to the plane of the marker movement. (The marker is supposed to move along a plane.) The frame rate of the camera is 100 frames/s; the IR flash is 1 ms long. Calculate the maximum displacement of the marker during the flash.
2. Calculate the maximum marker displacement of the marker between two frames according to problem 1.
3. During the studied movement the marker moves in the horizontal plane. The horizontal length of the FOV of the camera is 1 m. The uncertainty of marker image centre point estimation is 1:6000. Calculate the maximum flash duration during which the marker displacement is not greater than distance related to centre point estimation uncertainty. (Maximum marker velocity is the same as in problem 1)
4. Calculate the refraction coefficient of the marker material to air so that incident light is reflected to the same direction where it comes from (see Figure 10.9).
5. A three dimensional acceleration meter senses the following momentary values: $\mathbf{a}_z$ (vertical) = 0.707 g; $\mathbf{a}_x$ = 0.707 g; $\mathbf{a}_y$ = 0 g. Specify at least two different movements that produce these values.
6. Compare the active and passive marker based movement analysis.
7. How do we calibrate marker based motion analysers?
8. Give a method to characterise quasiperiodic human movement.
9. How would you measure the resolution and accuracy of a marker based motion analyser?
10. What is the usual result on hand tremor when the tested persons close their eyes?

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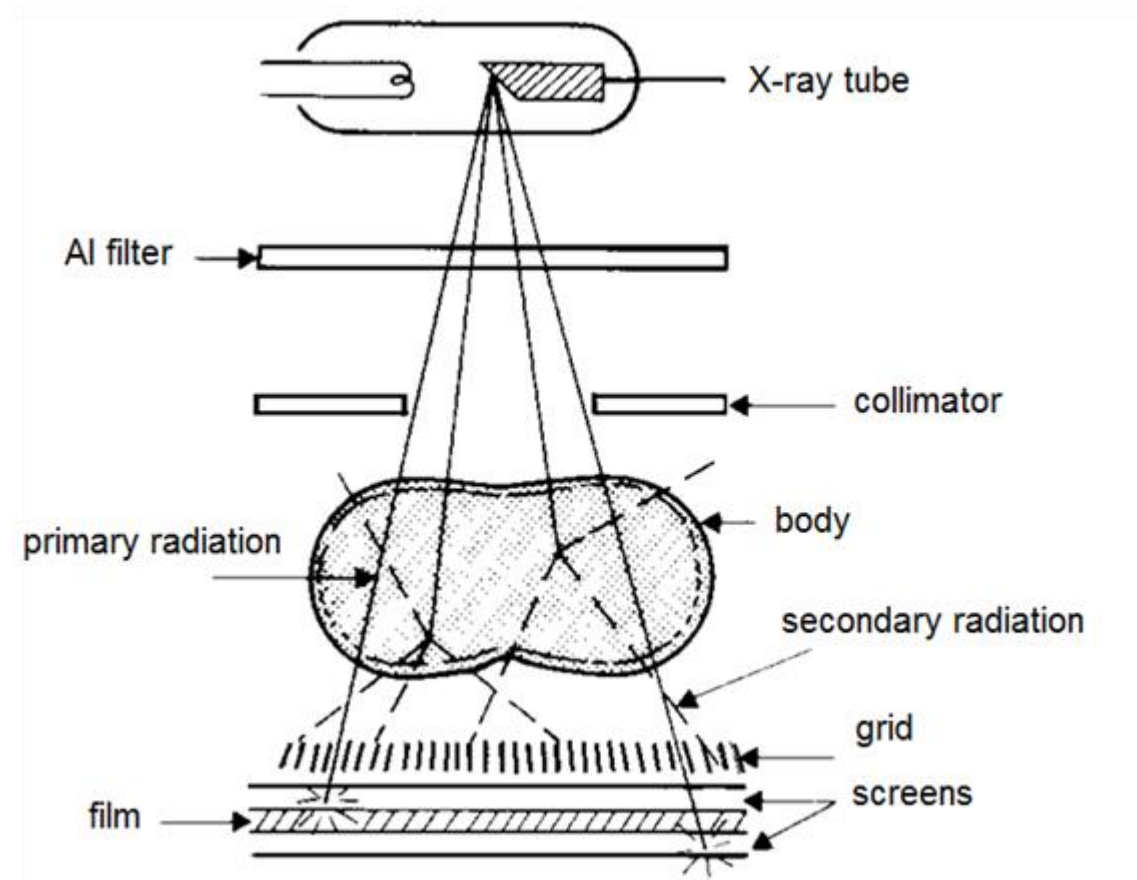
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Chapter 11. Medical imaging

1. X-ray based imaging

Initially medical imaging could only visualise the anatomical structure of the human body. The first image was taken by W. C. Röntgen. The formerly unknown ray was named to remember him (in English it is even today called X-ray). Figure 11.1 shows the operating principle of the X-ray machine.

Figure 11.1. The operating principle of the X-ray machine (Based on Siedband MP: Medical Imaging Systems Figure 12.5; <http://www.unc.edu/~finley/BME422/Webster/c12.pdf>)



The big calcium molecules in the bones absorb X-ray. The shadow of a bone masks all other organs that are in the path [10.9]. Conventional x-ray machines are unable to visualise e.g. the brain. Figure 11.2 shows the first X-ray image ever made: the hand of Röntgen's wife with a ring on her finger. Figure 11.3 shows another X-ray image taken by Röntgen a year later, in 1896. Image quality improved substantially.

Besides analogue imaging on film digital imaging is more and more frequent. Processing of several digital images further information is available by computing (this explains the name computed tomography, CT).

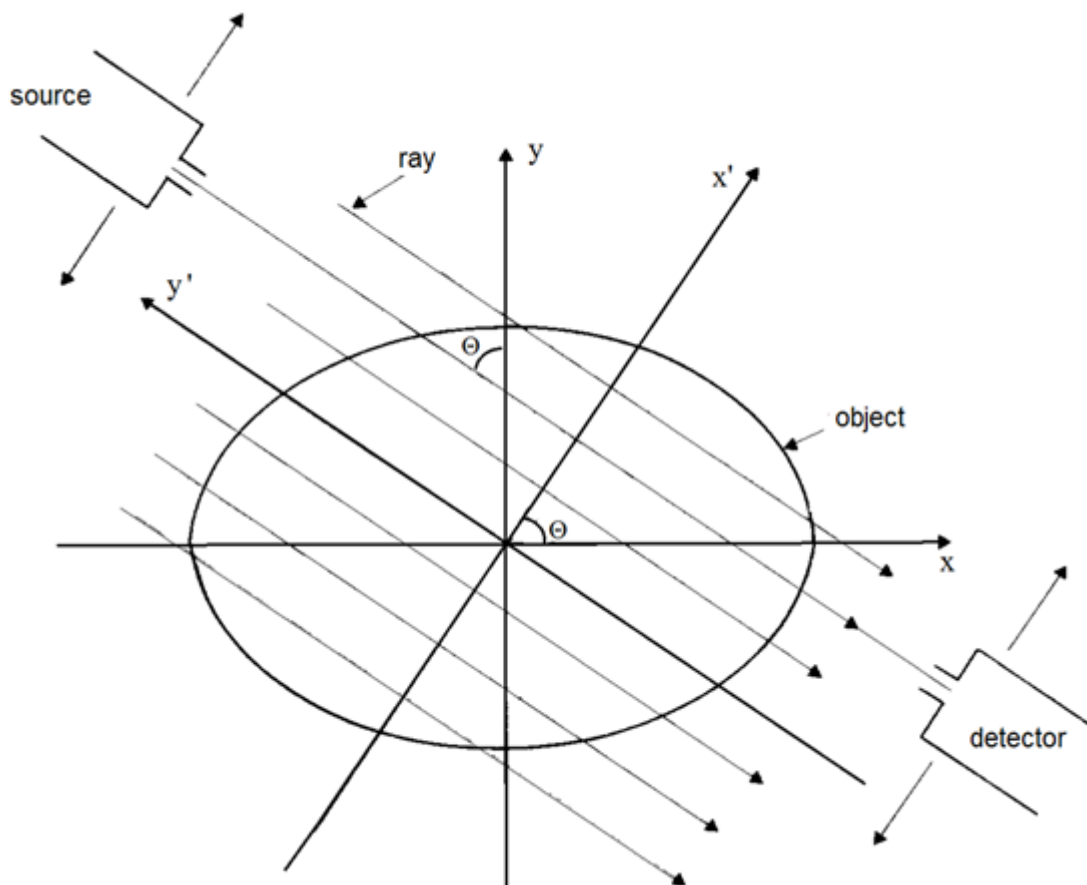
Figure 11.2. The first röntgen (X-ray) image made by W.K. Röntgen of his wife's hand (1895) (Wikimedia Commons, First medical X-ray by Wilhelm Röntgen of his wife Anna Bertha Ludwig's hand - 18951222.jpg)



Figure 11.3. Image made by W. K. Röntgen of A. Kölliker's hand, 1896 (Wikimedia Commons, X-ray by Wilhelm Röntgen of Albert von Kölliker's hand - 18960123-02.jpg)



Figure 11.4. The principle of computed tomography, CT (Based on Siedband MP: Medical Imaging Systems Figure 12.11, <http://www.unc.edu/~finley/BME422/Webster/c12.pdf>)



The principle of computed tomography (CT) is shown in Figures 11.4 – 11.6. The mathematical model was elaborated by Radon. The first functioning device was constructed by Hounsfield and Cormack who were later awarded with Nobel Prize for this. Figure 11.4 shows the collection of information. The source and the detector assign a straight line. The coplanar segment of the body to be analysed is scanned. The scanning beam is turned by a few degrees between two scans. When imaging the brain it influences only by about 1% the attenuation; 99% is determined by the skull. Even though computing the attenuation along a number of straight lines the attenuation of the skull can be eliminated.

Figure 11.5. Principle of computing tomography (CT) (Based on Siedband MP: Medical Imaging Systems Figure 12.12; <http://www.unc.edu/~finley/BME422/Webster/c12.pdf>)

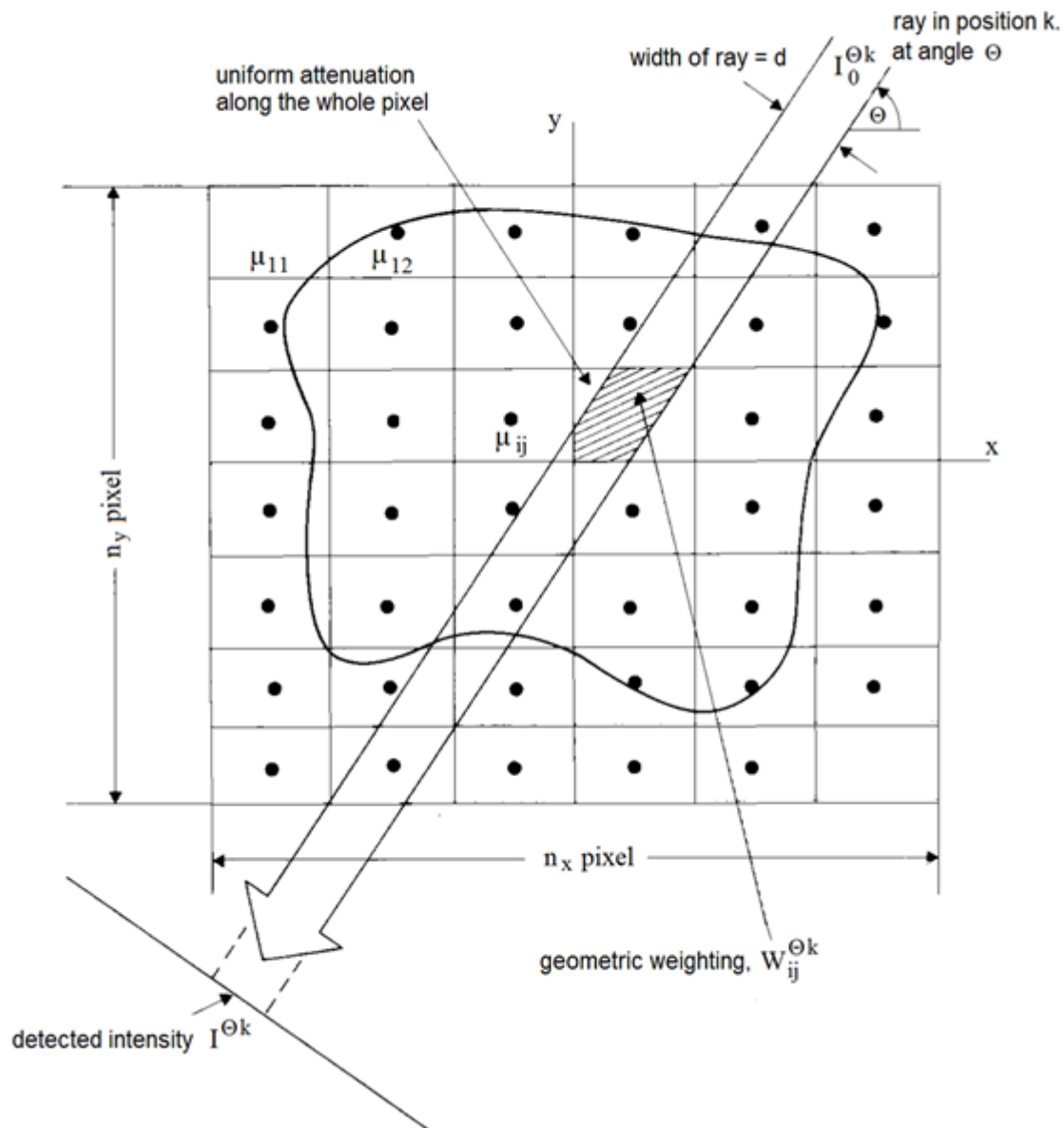


Figure 11.5 shows one possible computation. The image field is divided into pixels (c_{ij}) and an initial value of attenuation (μ_{ij}) is assigned to each pixel. It is assumed that the attenuation of pixels along a straight line add up. The solution of the resulting equation system gives the μ_{ij} attenuations. Based on them the image can be drawn: the greater is the computed attenuation of a pixel the darker it is in the image.

Back projection can also be applied. From the sensor along the straight line the detected intensity is projected back. The simplest algorithm assigns the same attenuation to each pixel along the straight line. Along all straight lines that were used in scanning the detected intensity is projected back and for every pixel these attenuations

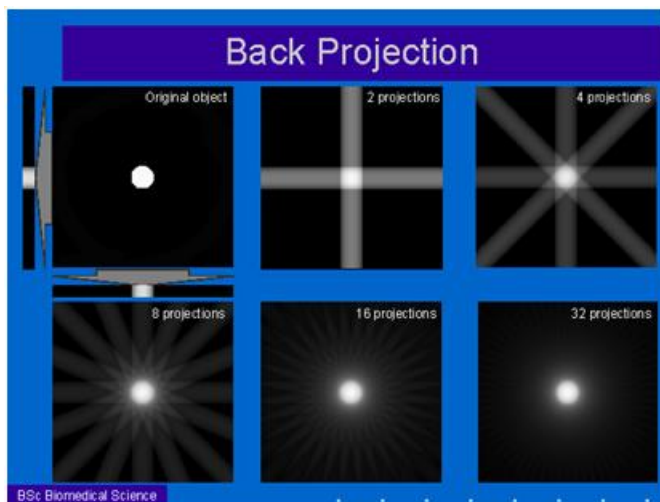
are added up. This simple algorithm gives blurry image thus different filtering algorithms (not detailed here) are applied before projecting back. Back projection is illustrated by the animation:

<http://project.mit.bme.hu/kobak2012/backprojection.pps>

The method can be extended to three dimensional imaging. This requires two dimensional imaging in a number of parallel slices. The resolution of CT is better and better because both the sensors have more pixels and the image processors are more powerful. In 1995 the maximum resolution was 512 x 512. Today 1024 x 1024 is available. Evaluation of CTs requires several parameters to be considered. Spatial resolution is characterised by the line pairs/cm. Today this value can reach 20.

The time of a two dimensional CT image generation is mainly determined by the scanning speed of the source – detector pair. Stepping is usually done in 1° rotations until 180° is reached. First generation CTs took around 20 s to generate an image.

Figure 11.6. The principle of back projection
<http://www.impactscan.org/slides/xrayct/sld018.htm> (From the training material of ImaptScan group)



Modern CT devices apply a number of sources and detectors so they are able to make 10 images/s. This is enough to analyse the motion of organs (e.g. heart). The first generation CT contained one source and one detector; they were turned around the patient by 180°. Imaging of one slice took several minutes. Second generation CTs contained one source but several detectors. A 10° fan-shaped part was scanned in parallel. It took about 20s to complete one slice. Third generation CTs contain 500 – 1000 detectors; the fan-shape covers the whole slice. The source and the detector need not be stepped only rotated. One slice is ready in 0.5 s. Fourth generation CTs may contain 5000 detectors which are in fix position. Only the source rotates [11.1]. In fifth generation CTs the sources do not rotate either. One slice is ready in 50 ms.

Image processing greatly helps extracting the organ from the background. Thus it helps reveal deviations. Figure 11.7 shows that by subtracting the image made before filling in contrast material from the image made after that (B-A) the vessels can be analysed much easier than without subtraction (B). The method is called DSA (digital subtraction angiography). It must be assured that the patient remains in the same position before and after filling the contrast material. Figure 11.8 shows an image of the vessels in the brain (cerebral angiogram) taken by applying the DSA method.

Figure 11.7. The principle of the DSA method
<http://www.droid.cuhk.edu.hk/web/service/angio/dsa.htm> (author: The Chinese University of Hong Kong, Department of Imaging and Interventional Radiology)

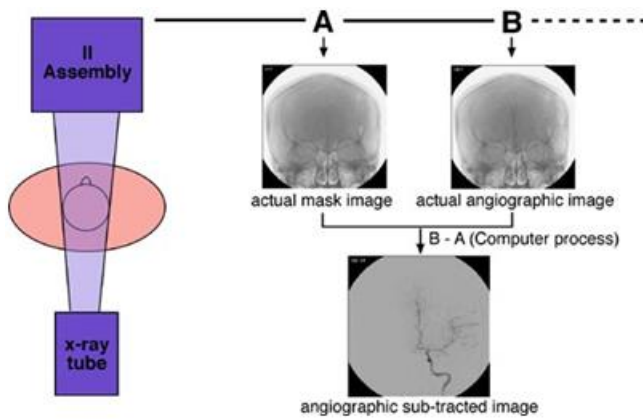
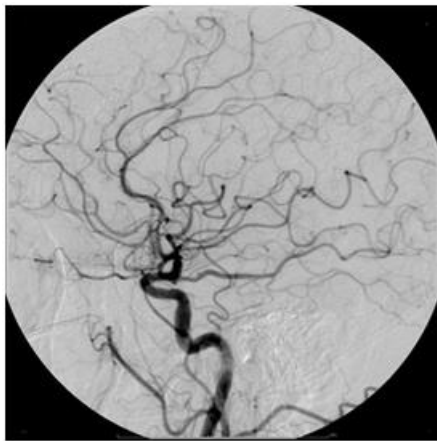


Figure 11.8. Vessels in the brain (DSA image)
http://commons.wikimedia.org/wiki/File:Cerebral_Angiogram_Lateral.jpg (author: Glitzy queen00)



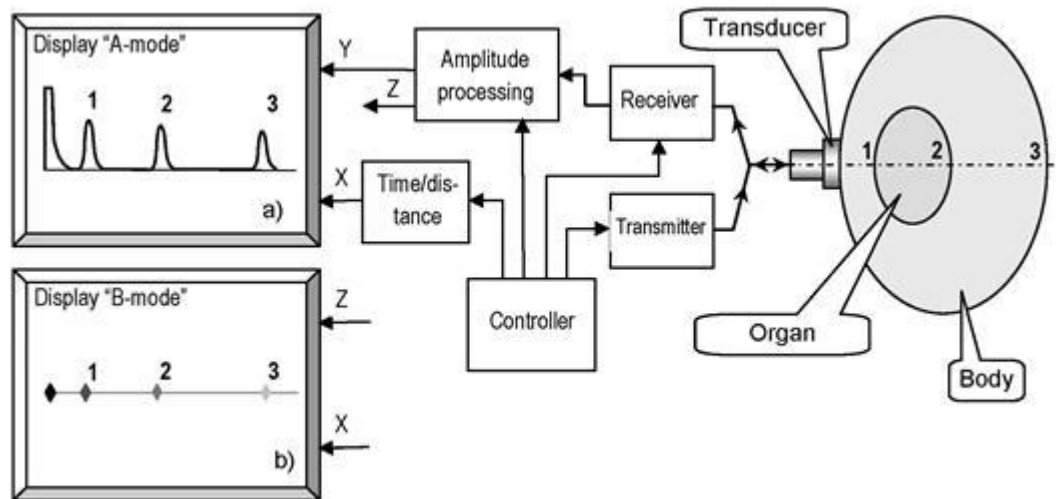
2. Ultrasound imaging

2.1. Processing and displaying the echo

Early devices displayed the echo in real time by using oscilloscopes. The block diagram of the necessary hardware is shown in Figure 11.9 [11.10], [11.11]. The amplifier in the receiver usually has time gain control (TGC) which increases the gain in time following the transmission. The amplitude of the echo is the smaller the farther is the reflecting object. The smaller is the amplitude the greater gain is needed. Most often the TGC has logarithmic characteristics.

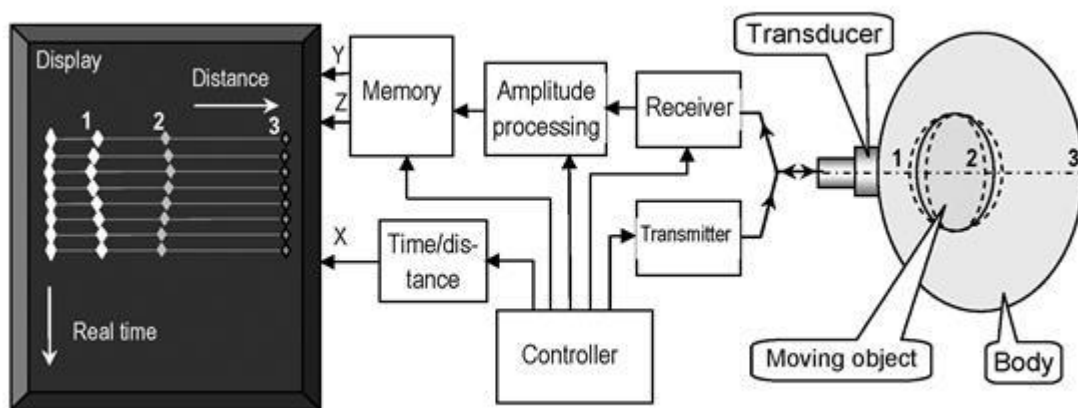
By demodulating the echo the amplitude processing unit generates the envelope which controls the vertical (Y) deflection. The B (brightness) mode requires the envelope to be used to control the brightness of the oscilloscope (called Z input). This mode is especially applicable for two dimensional display or when motion is pictured.

Figure 11.9. Simplified block diagram of a line scanner. Vertical (Y) deflection is controlled by the demodulated echo amplitude, A display mode (a). Brightness modulation, B display mode (b)



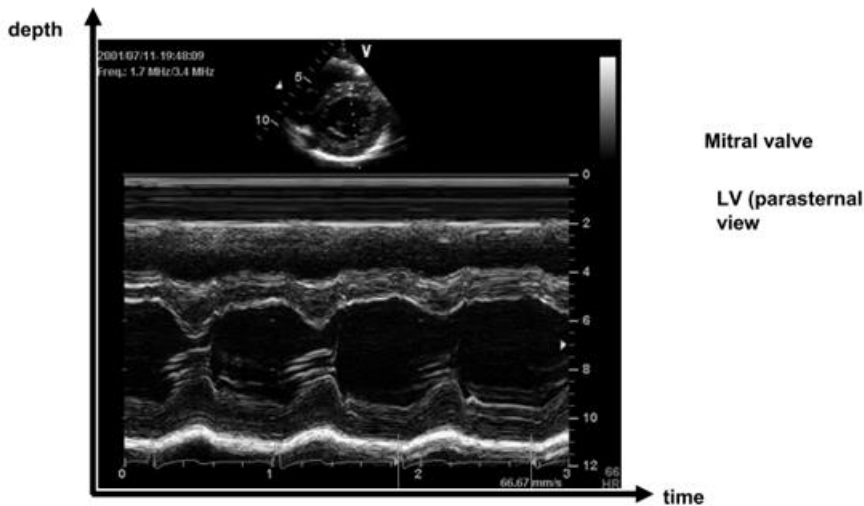
Motion (**M**) or Time Motion (**TM**) is used to analyse moving organs (e.g. the heart). In this mode the transducer is fixed. The displacement of the observed organ (its border lines) along the beam line is displayed. The display mode requires memory that stores several echoes. These are pictured on the display one below the other, see Figure 11.10.

Figure 11.10. The simplified block diagram of an ultrasound line scanner displaying the movement of an organ (M or TM mode)



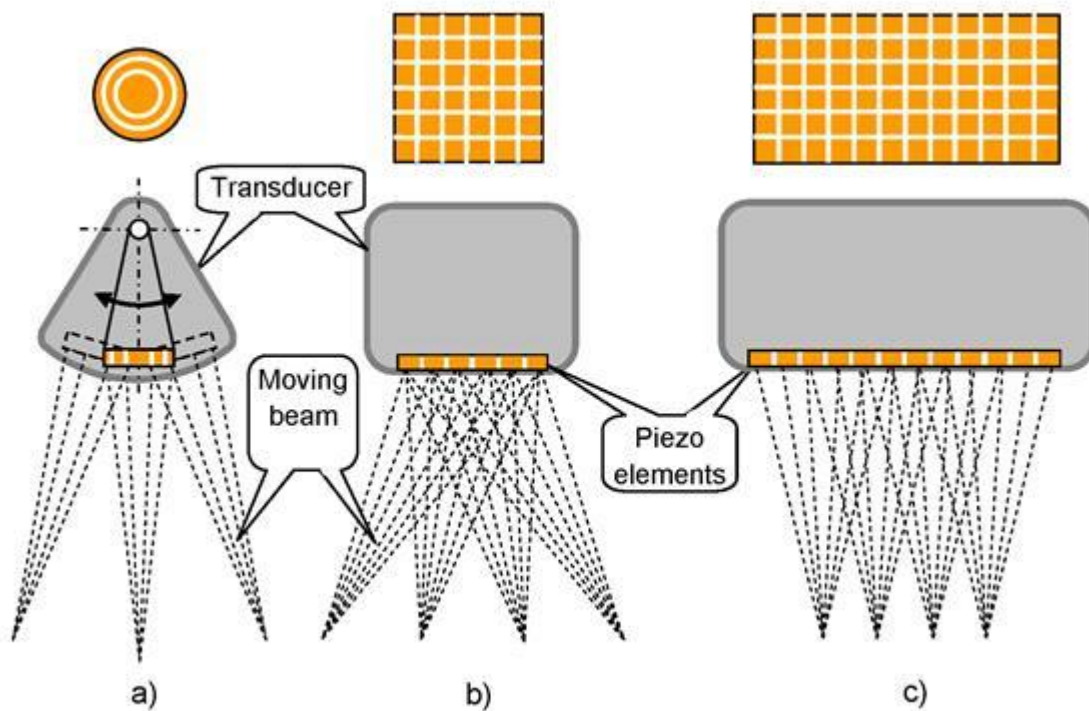
This method pictures movement in a still image which is far simpler to be evaluated by the human observer. Figure 11.11 shows a three second ultrasound record picturing the movement of the mitral valve.

Figure 11.11. Picturing the movement of the mitral valve in still image using the TM mode of an ultrasound line scanner
<http://www.dtic.upf.edu/~afrangi/ibi/UltrasoundImagingBW.pdf> (author: Alejandro Frangi)



2.2. Generation of multidimensional images

Figure 11.12. Realisations of planar scanning: the transducer rotates within the sensor head (a); the beam is deflected by applying time delays (b); the beam scans horizontally by shifting the activation of the piezo elements (c). All three realisations use dynamic focusing. Frontal arrangement of the piezo elements are shown above



Ultrasound beam produces an echo (one dimensional) of the borderlines between different tissues along a line. The propagation time determines the time needed to get an echo. A 15 cm deep line scan takes about 200 μ s. Thus, several thousand line scans can be completed in one second. The planar image (two dimensional) is assembled by storing the B mode line scans [11.11]. The spatial direction of the line is required for assembling the image. The early planar scanning required manual movement of the sensor head. It was difficult to determine the spatial direction of the scanning beam and transferring this information to the display controller. Figure 11.12 shows automatic planar scanning methods. The transducer is rotated by a motor within the sensor head (a). The sensor head is filled with oil to eliminate air gaps. (b) and (c) show how the beam direction can be changed without mechanically moving the piezo elements. (b) illustrates the planar scanning by applying time

delays between exciting the piezo elements. The number of piezo elements shown in (c) can be 100 of which always a few are active to produce the focused beam in the desired direction. The set of excited elements is shifted by one thus shifting the beam in parallel. Two dimensional images are displayed on universal digital monitors.

3. Magnetic resonance imaging (MRI)

Magnetic resonance imaging (MRI) most often displays the distribution of hydrogen molecules in the examined body segment [11.2], [11.3]. This correlates well with the structure of the body because it is made up of 60% water. The distribution of water is not homogeneous: 20% in fat tissues, 25% in bones, 70% in liver, 75% in muscles, 80% in blood and may reach 85% in the brain. Contrary to X-ray images the shadow of bones does not mask soft tissues. The nucleus of hydrogen (^1H) contains a positively charged proton. Each proton has spin acting like a magnetic dipole. The direction of the spin is random. When strong magnetic field is applied then the direction of the spin for the majority of protons becomes parallel with the magnetic field (for a few it becomes antiparallel). The direction of the spin of a proton is not constant; it precesses (see Figure 11.13). The frequency of precession is called Larmor frequency (ω). Its value depends on the magnetic field strength (B) and the gyromagnetic constant (γ), see eq. 11.1.

$$\omega = \gamma B \quad (11.1)$$

For ^1H : $\omega/2\pi = 42.58 \text{ MHz/T}$. This means that when the magnetic field strength is 1 T then the frequency of precession is 42.58 MHz.

Figure 11.13. The precessing movement of the proton



The usual notation is that the strong magnetic field (B) is in the vertical direction (z). When protons get RF radiation of Larmor frequency perpendicular to their spin they become excited, the direction of their spin changes by 90° to the x,y plane. While RF radiation exists the spin of a proton precesses at a small angle to the x,y plane. When RF radiation is switched off protons get back to their resting state; their spin pointing to z direction. Protons emit radiation when they get back to their resting state. Mapping of the distribution of hydrogen molecules is based on the detection of this radiation. The resultant radiation of all protons can be measured. *Scanning a slice of the body or of an organ is done by modulating the magnetic field strength in x , y and z direction.* By this modulation a small volume (voxel) is defined. Magnetic field strength can be modulated in one direction even during RF excitation. This makes possible the evaluation of radiation of protons along a line in parallel because the slightly different magnetic field results in slightly different radiation frequency. Parallel processing speeds up image generation. Figure 11.14 shows a slice taken from the head.

Changing the magnetic field strength and the RF frequency make possible the measurement of the distribution of other atoms as well (e.g. ^{31}P , ^{13}C , ^{15}N , ^{19}F).

Figure 11.14. A slice taken from the head by MRI
(http://commons.wikimedia.org/wiki/File:MRI_head_side.jpg; author: Ranveig Thattai)

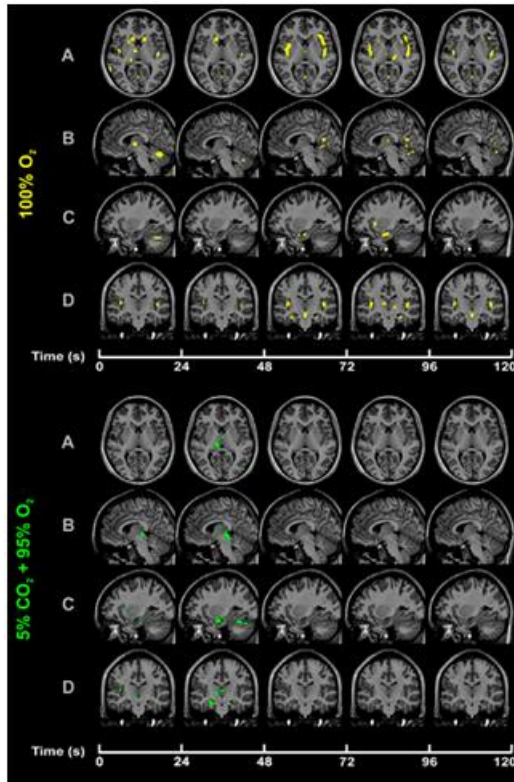


An MRI examination – depending on the volume of the studied body segment and the required resolution – lasts for 15 – 45 minutes. The slice thickness is between 0.5 and 10 mm, the maximum resolution within one slice is

presently 0.02 mm. As a general rule patients with pacemaker should not be tested with MRI because of the strong magnetic field. The applicability of MRI for patients with different implants must be thoroughly analysed [11.6].

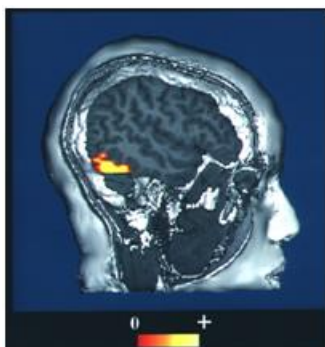
MRI devices have reached the speed needed for examining hemodynamic changes in the observed organ. This can be applied for the brain or for the spinal cord; at present with coarse resolution (3 mm). This examination method is called functional MRI (fMRI) [11.4]. One image/s is possible with 1 – 5 mm³ spatial resolution.

Figure 11.15. fMRI image series showing the brain activity changes activated by oxygen and carbon dioxide concentration variation [11.5]
(<http://commons.wikimedia.org/wiki/File:CO2-O2-fMRI-all-over-time.png>)



One image per second is not enough to assess brain processes. The parallel application of EEG (poor spatial and excellent temporal resolution) and fMRI (very good spatial and poor temporal resolution) is an effective procedure to measure brain activity [11.7]. Figure 11.16 shows which part is active in the brain of a person involved in face recognition.

Figure 11.16. fMRI taken from a person involved in face recognition. The increased blood supply of the visual cortex can be seen.
(http://commons.wikimedia.org/wiki/File:Face_recognition.jpg; author: NIH)



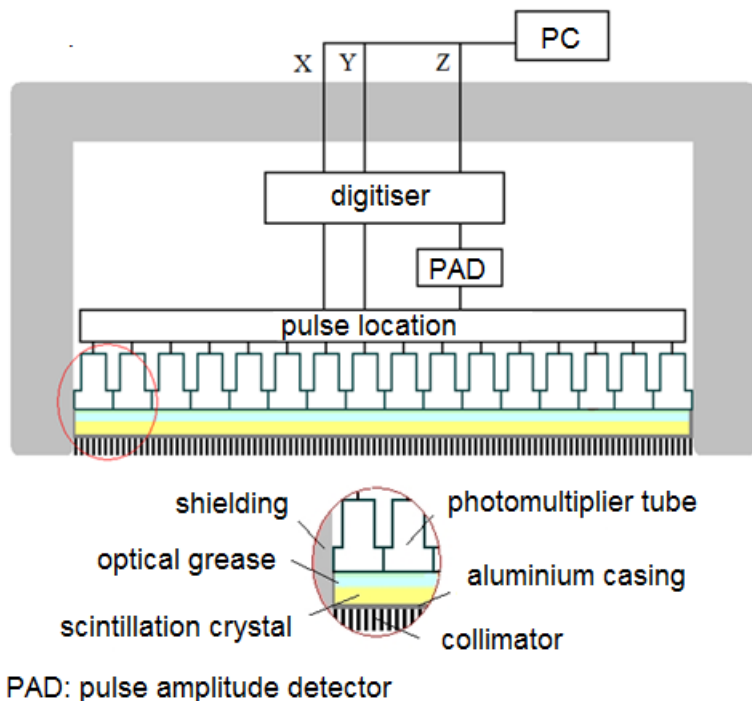
4. Imaging organ functions

Organ functions are often tested by injecting different markers into the body and analysing their distribution. Injected radioactive markers can be traced easily by detectors outside the body. For this purpose radioisotopes with short half-lives are injected into the blood stream. The isotopes are often generated locally. The distribution of the isotopes reflects the intensity of metabolism. In tumour cells the increased metabolic activity results in high radioactive isotope concentration. Positron emission tomography (PET) produces a three dimensional image of a functional process in the body. The distribution of radioactive isotopes is determined by detecting pairs of gamma rays emitted when a positron from the isotope encounters an electron annihilating both of them. The two gamma rays move in opposite directions. The time difference between the incidences of the rays to the sensor ring (see Figure 11.19) determines the site where the annihilation occurred. Table 11.1 gives the half-life of isotopes frequently used for PET scans. The half-lives are short thus they mean minimal threat to the patient. F18 FDG (fluorodeoxyglucose) is also often used as marker.

Table 11.1. Half-life of isotopes applicable in PET analysis

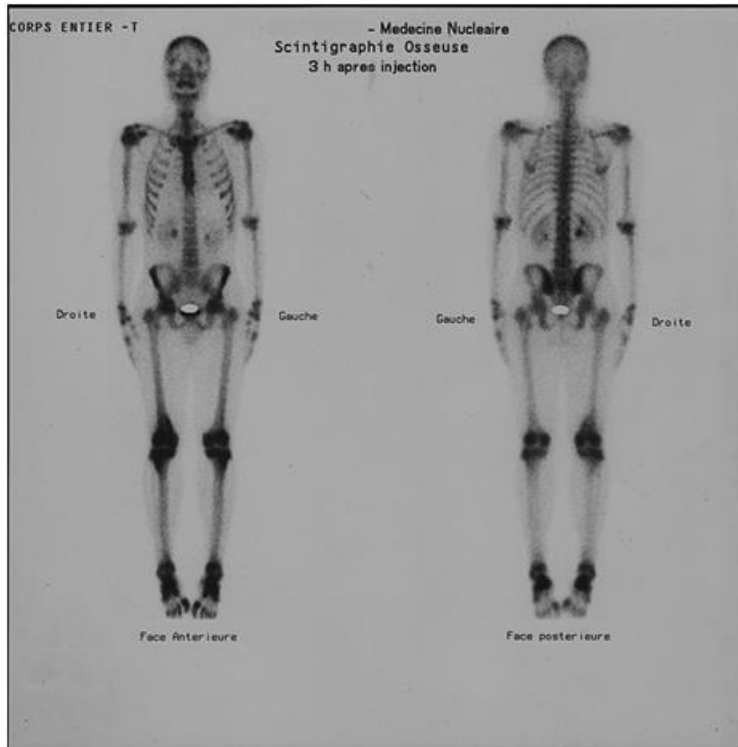
isotope	half-life (minute)
^{18}F	110,0
^{11}C	20,4
^{13}N	10,0
^{60}Ga	62,3
^{82}Rb	1,3

Figure 11.17. Structure of the gamma camera (based on Wikimedia Commons Gamma Camera Cross Section.png and Gamma Camera Cross Section Detail.png)



Radiation emitted by radioactive isotopes can be detected by gamma camera [8g, see Figure 11.17. Other sensors capable of measuring radioactive radiation are similar to the gamma camera. Figure 11.18 shows an image of the whole body taken by a gamma camera.

Figure 11.18. Whole body image taken by a gamma camera. Left: supine; right prone position. (http://commons.wikimedia.org/wiki/File:Scintigraphie_corps_entier.jpg; author:Grook Da Oger)



The positron emission tomography is illustrated in Figure 11.19. Figure 11.20 shows different sensor arrangements. Figure 11.21 shows a PET/CT image taken from a patient suffering from severe vasculitis.

Figure 11.19. Operation principle of PET (<http://commons.wikimedia.org/wiki/File:PET-schema.png>, author:Langner J)

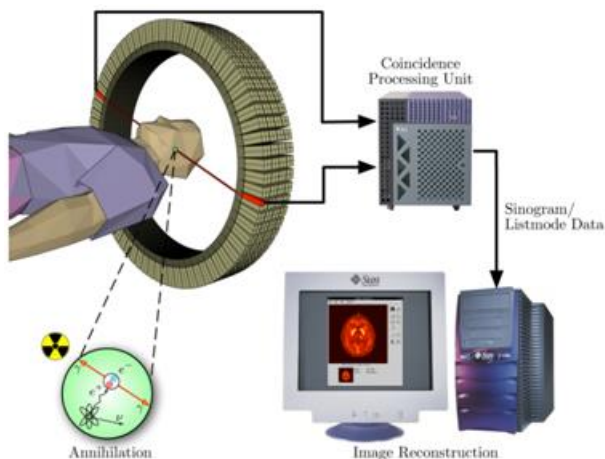


Figure 11.20. Development of PET sensors: (a) and (b) rotating; (c) static sensors

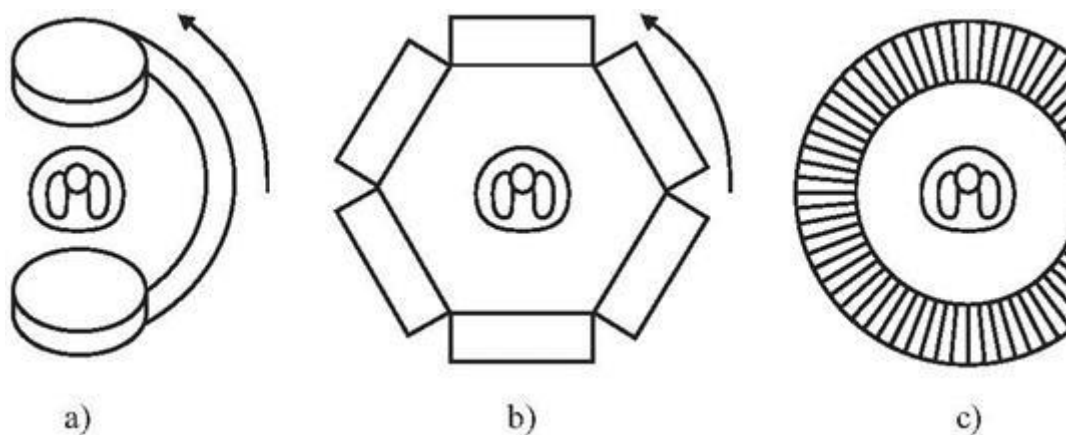
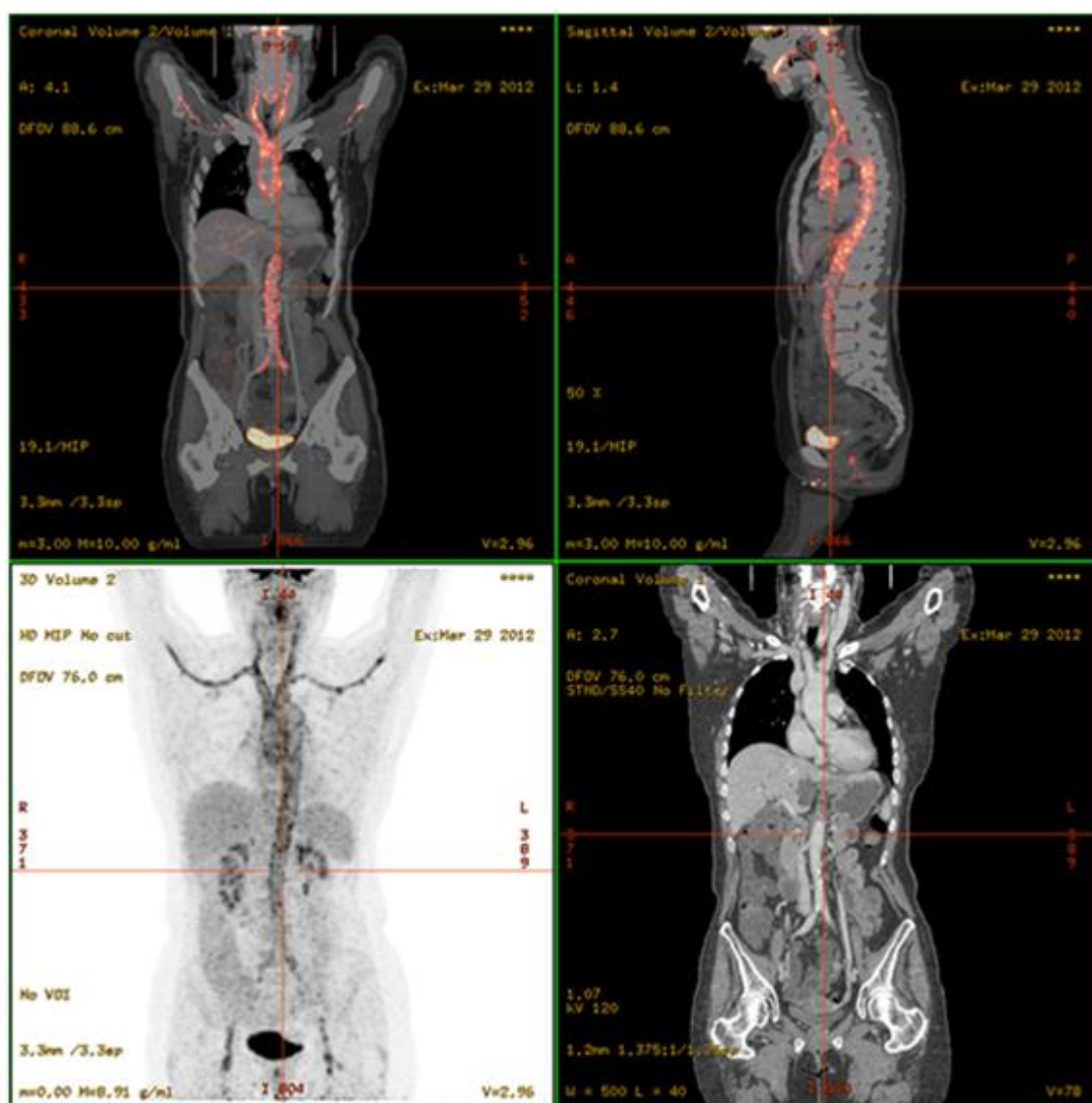


Figure 11.21. PET/CT showing severe vasculitis
 (http://commons.wikimedia.org/wiki/File:PET-schema.png; author: Hg6996)



Single photon emission computed tomography (SPECT) uses marker which directly emits gamma rays. Comparing it to PET SPECT is cheaper but its resolution is worse (1 cm is typical).

5. Devices

Figure 11.22 shows a cold cathode X-ray tube. Such tubes were applied in the early period (until 1920).

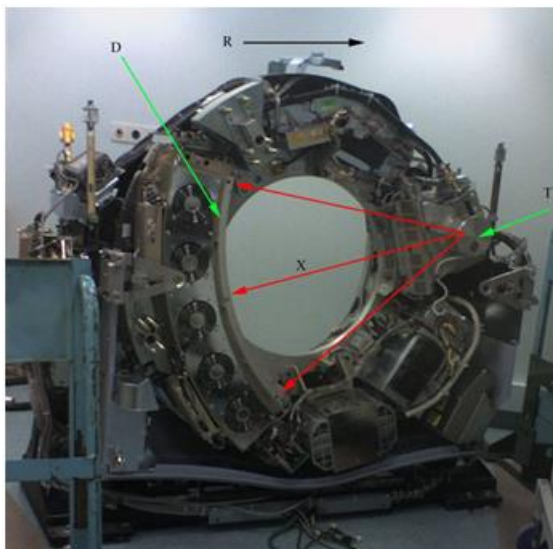
Figure 11.22. Cold cathode X-ray tube (http://commons.wikimedia.org/wiki/File:X-ray_tube_3.jpg; author: Aida)



Figure 11.23. Modern dental X-ray device (http://commons.wikimedia.org/wiki/File:Dental_X-Ray.jpg; author: Desire C)



Figure 11.24. Construction of a third generation CT. T X-ray tube, D: detectors, X: X-ray, R: direction of gantry rotation. (<http://commons.wikimedia.org/wiki/File:Ct-internals.jpg>; author: Bjecas)



The rotation of the gantry can be seen on the video:

<http://commons.wikimedia.org/wiki/File:CT-Rotation.ogv>

The flow distribution in the aorta is illustrated on an animation made using the images taken by an MRI (10 images were taken in a second).

http://commons.wikimedia.org/wiki/File:Rt_mri_flow_aorta_27fps.ogv

(The links were active on 19th April, 2013.)

Figure 11.25. CT device
(http://commons.wikimedia.org/wiki/File:64_slice_scanner.JPG; author: ToNToNi)



Figure 11.26. MRI device
(http://commons.wikimedia.org/wiki/File:Modern_3T_MRI.JPG; author: Braegel)



Figure 11.27. Ultrasound image of a gallstone
(http://commons.wikimedia.org/wiki/File:Ultrasound_image_of_gallbladder_stone_Gallstone_091937515.jpg; author: Nevit Dilmen)



Figure 11.28. Paediatric echocardiography with ultrasound imaging (http://commons.wikimedia.org/wiki/File:Sonographer_doing_pediatric_echocardiography.JPG; author: Ekko)



Figure 11.29. Ultrasound image of a foetus (http://commons.wikimedia.org/wiki/File:Ultrasound_image_of_a_fetus.jpg; author: Biagio Azzarelli)



Figure 11.30. SPECT device (http://commons.wikimedia.org/wiki/File:SPECT_CT.JPG; author: Ytrottier)



6. Problems

1. An ultrasound imaging device operates with 1 MHz frequency. The transmitted signal contains 10 periods. The propagation velocity of ultrasound in the body is 1500 m/s. Calculate the depth of the dead space.
2. We want to measure with ultrasound to 11 cm deep in soft tissue. The measuring frequency is 3 MHz, the average attenuation of the soft tissue is 0.8 dB/(cm×MHz). Calculate the necessary change in the gain of the receiver to produce the same amplitude at the output of the TGC amplifier for an echo from 1 cm and 10 cm (A_{v10cm}/A_{v1cm}).
3. In the soft tissue in problem 2 the sound speed is 1550 m/s. Calculate the time delay from transmission to the moment when the gain must be A_{v1cm} and when A_{v10cm} .
4. In Figure 11.10 (to the left) a schematic, in Figure 11.11 a real TM mode image can be seen. Compare the two images and interpret their coordinate system.
5. Figure 11.27 shows a gallbladder containing a gallstone (two dimensional cross section). What were the directions of the scanning ultrasound lines? Why can't we see echo from the inside of the gallstone? Why is the area behind the stone darker than its surroundings? Why are there lighter areas behind the bladder?
6. What difference can be seen between the upper and lower part of the image in Figure 11.27 regarding the lateral resolution? Explain the difference.
7. During abdominal examination echoes are detected from boundaries being 6 and 8 cm far from the ultrasound sensor. The attenuation between the sensor and the boundaries is 3 dB/cm. Calculate the ratio of the echo amplitudes reflected from 6 and 8 cm.
8. For abdominal examination 2 MHz ultrasound is used. Is it possible to detect a sphere shaped gallstone with 1 mm diameter?
9. How should be decided if MRI imaging is possible of a patient with (a) hip prosthesis, (b) pacemaker, (c) dental prosthesis (bridge)?
10. Compare the PET-CT and MRI imaging technique.

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